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ABSTRACT

Flash talks (FT)

Flash talks on food allergy in children

000417 | Cashew allergy starts in toddler age with high risk of anaphylaxis: A multicenter cross-sectional study with 222 subjects

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Background: Tree nut is becoming an increasingly prevalent cause of food allergy in Western countries, and is a common cause of anaphylaxis. There are no studies on the onset of children with cashew allergy. In this study, we aimed to describe the clinical features of the onset of cashew allergy in Japanese pediatric population.

Method: We conducted a multi-center cross-sectional study and retrospectively collected clinical data of children with cashew allergy from medical charts. Patients aged 0 to 15 who visited the participating institutions between 2013 and 2022, with a clear history of immediate reaction with cashew ingestion and confirmed cashew sensitization on blood tests were included. Information on the patient's initial reaction with cashew ingestion, background, allergic comorbidities, and serological data was obtained. The primary outcome was the age of the initial reaction.

Results: A total of 222 patients were included in this study. The median age of the initial reaction was 5 years (interquartile range: 3–7 years). The median level of specific IgE to cashew and Ana o 3 within a year of the initial reaction was 7.8 kU_A/L (interquartile range: 2.9–27.6 kU_A/L) and 6.9 kU_A/L (interquartile range: 1.8–20.9 kU_A/L). The rate of infantile eczema, atopic dermatitis, bronchial asthma or recurrent wheeze, and allergic rhinitis were 43% (89/222), 54% (112/222), 23% (47/222), and 38% (79/222), respectively. History of immediate reaction to other foods prior to cashew was seen in 71% of the patients, and the most common causative foods were walnut, egg, milk, peanut, and wheat. Sensitization to cashew was confirmed before the initial reaction in 28% of the patients, and the initial reaction occurred during oral food challenge (OFC) in 21% of the patients. During the initial reaction, cutaneous, mucous, gastrointestinal, respiratory, and cardiovascular symptoms were seen in 70%, 52%, 56%, 32%, and 11% of the patients, respectively. Anaphylaxis occurred in 32% of all initial reactions and in 17% of initial reactions during OFCs.

Conclusion: In Japanese children with cashew allergy, the initial reaction occurred most during early childhood, and anaphylaxis was common. Further investigation is required to develop a method to identify children at high risk of cashew allergy.

Conflicts of interest: The authors did not specify any links of interest.

000255 | Perinatal exposure to TIO_2 nanoparticles increases the progeny's proclivity to develop food allergy

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Background: Food allergy (FA) is an inappropriate and excessive immunological response against food proteins that results from a defective establishment of oral tolerance. Various environmental factors may act from an early age, or even from *in utero* life, to promote the development of this pathology. Indeed, the perinatal period is a critical window of susceptibility during which stressors such as chemicals can affect the establishment of intestinal homeostasis, favoring the onset of immune related-diseases such as FA. Among them are foodborne inorganic nanoparticles (NPs) such as titanium dioxide (TiO_2), known for their potential adverse immune effects in the gut. Moreover, TiO_2 NPs have been demonstrated to cross the human placental barrier and to be excreted in milk, possibly interfering with the establishment of gut homeostasis in early life. In the present study, we aimed to determine the impact of perinatal exposure to food-grade TiO_2 on the propensity of the progeny to develop FA.

Method: Female mice were exposed to a control or food-grade (*fg*)-TiO_2-enriched diet at a human relevant level (10 mg/kg BW/day) starting before and continuing during pregnancy and lactating periods. At weaning, pups were fed with the same diet as their mother. Progeny from both groups was then experimentally sensitized to cow's milk (CM) proteins thanks to weekly intra-gastric

administrations of CM with *Cholera toxin*. In a subgroup, oral tolerance to CM was induced before sensitization. Sensitization was then assessed by measuring levels of b-lactoglobulin (BLG) and casein-specific IgG1 and IgE antibodies in plasma collected after an oral food challenge (OFC) with CM concentrate. Elicitation of the allergic reaction was checked by measuring mouse mast cell protease (mMCP1) concentrations.

Results: Male but not female offspring perinatally exposed to *fg*-TiO_2 exhibited higher plasmatic levels of mMCP-1 after the OFC compared to controls, indicating a higher elicitation of the intestinal allergic reaction in this sex only. Moreover, whereas oral tolerance was efficiently developed in controls and in perinatally exposed females, it was less efficient in exposed male progeny, as demonstrated by BLG- and casein-specific IgE and IgG1 levels.

Conclusion: These results suggest that dietary chronic exposure to *fg*-TiO_2, starting *in utero*, significantly interfere with the induction of oral tolerance and enhance the propensity to develop FA, with a clear gender effect.

Conflicts of interest: The authors did not specify any links of interest.

000993 | Stratifying risk for milk allergies utilizing EMR data: A machine learning approach

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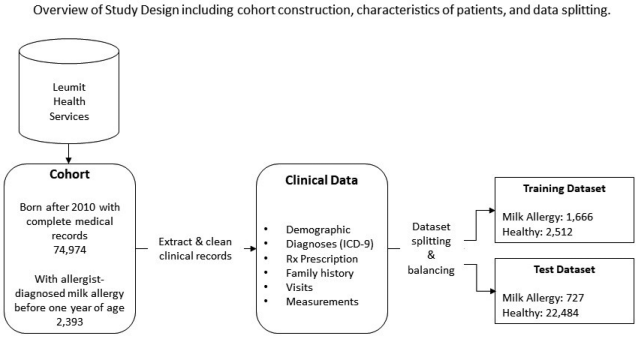
*Presenting author: T. Landau

Background: The prevalence of food allergy has grown globally and cow's milk is one of the most common causes of allergic reactions to food and of food-induced anaphylaxis. Dietary practices, along with genetic, environmental, and medical history features affect one's risk of developing food allergies. It is currently unclear as to whether the combined analysis of these risk elements may allow us to understand the driving factors behind an infant's risk of developing cow's milk allergy. We aimed to develop various prediction models to stratify an infant's risk of developing cow's milk allergy from a large and nationally representative healthcare provider electronical record database.

Method: We performed a retrospective, cross-sectional database study on the Leumit Health Services electronic medical record database. Patients born after 2010 and diagnosed with milk allergy by an allergist before reaching one year of age were included (n = 2,393). Control patients included all patients born after 2010 without a food allergy diagnosis to date (n = 74,974). Documented risk factors include parental, sibling and infant history of atopic conditions, weight, gender, season of birth, socio-economic status, prescriptions, specialist visits and previous diagnoses. All factors were taken from the period prior to the milk allergy diagnosis. Logistic regression and machine learning predictive models were trained and tested on the combined dataset.

Results: The odds ratio conferred on an infant due to parental (1.33, CI 1.26–1.40, $p < 0.001$) or sibling (1.34, CI 1.29–1.40, $p < 0.001$) history of atopy and prior diagnosis of atopic dermatitis (2.73, CI 2.43–3.06, $p < 0.001$) constitute important risk factors. Receiver operating characteristic curve analyses showed an area under the curve of 0.74 for a logistic regression and 0.80 for a XGBoost model. The latter model boasts a maximum accuracy of 81%, with corresponding sensitivity of 64%, and specificity of 81%.

Conclusion: Machine learning predictive modeling using routinely collected electronic medical record data can serve as a powerful tool to stratify an infant's risk of developing cow's milk allergy. Knowledge of an infant's risk can inform both caregivers and medical professionals as to timely interventions to mitigate the development of cow's milk allergy.



Conflicts of interest: TL, DG & MB report personal fees from MYOR Diagnostics Ltd. during the conduct of the study.

000645 | A novel intervention to support families managing both food allergy and lower income

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Background: Owing to the near-ubiquity of cow's milk in the food supply chain and higher costs of non-cow's milk alternatives, cow's milk allergy (CMA) has been described as the most burdensome food allergy. Although food costs have increased significantly during the COVID-19 pandemic, families managing food allergy are disproportionately burdened. We aimed to describe families' food costs and mental health during a 6-month biweekly home delivery of CMA-friendly meal kits.

Method: We recruited 10 families whose children <6 years had allergist-diagnosed CMA, and who had a net household income of <$70,001 Canadian dollars (approximately €48,900). At baseline, families completed a demographics questionnaire, including allergic history. Severe reactions were operationalised as reported dizziness/fainting, respiratory distress or arrest, or loss of consciousness. Every 2 weeks for 6 months (Feb-Jul 2022), we delivered CMA-friendly meal kits, valued at ~$50/kit (~€39/kit) to families' homes. Other reported food allergies were also considered when creating meal kits for families. At baseline, midpoint and endpoint, families completed questionnaires on food costs and mental health.

Results: Amongst the 10 participating families, the mean monthly income was $3493.81 (€2441.20). Families were ethnically diverse, and most were 4-person (range 2–8) families. At baseline, children with CMA were age 3.0 ± 1.4 years, and 20% had a history of severe reactions. Other food allergies were reported, most commonly to eggs, peanut and soy (n = 4 each).

At baseline, monthly food costs averaged $736.36 ± $387.36, which decreased at midpoint to $673.75 ± 201.28, representing a non-statistically significant decrease of $62.61 (€43.74), or 8.5%. By endpoint, these costs had rebounded to $712.50 ± $251.78, corresponding to an increase from midpoint of $38.75 (€27.06), or 5.4%, but which reflected a net decrease from baseline of $23.86 (€16.67), or 3.2%.

Regarding mental health, food allergy quality of life and perceived stress did not change during the intervention (all $p \geq 0.60$). Perceived life status non-significantly improved from baseline to midpoint (6.82 ± 0.48; and, 8.0 ± 0.46, respectively, p = 0.11), but at endpoint (7.48 ± 0.53), was comparable to baseline (p = 0.38).

Conclusion: During a period in which food costs increased by approximately 11% in Canada, a 6-month home delivery of CMA-meal kits resulted in a modest decrease in food costs, with little change to mental health.

Conflicts of interest: Elissa Abrams is an employee of the Public Health Agency of Canada; the views expressed are here own and not those of the Public Health Agency. Moshe Ben-Shoshan sits on the following advisory boards: Stallergenes Greer, Novartis, Sanofi; reports personal fees from Bausch Health, Stallergenes Greer, Novartis, Sanofi; grants from Stallergene Greer; and participated in Novartis, Aimmune Therapeutics, and Sanofi clinical trials. Jennifer Protudjer is Section Head for Allied Health, and a Member of the Board, for the Canadian Society of Allergy and Clinical Immunology; sits on the steering committee for Canada's National Food Allergy Action Plan, and reports consultancy for Nutricia, Novartis, and ALK-Abelló. The remaining authors have no conflicts of interest to report.

000141 | Factors associated with food allergy among preschool atopic dermatitis (AD) children and natural history of AD

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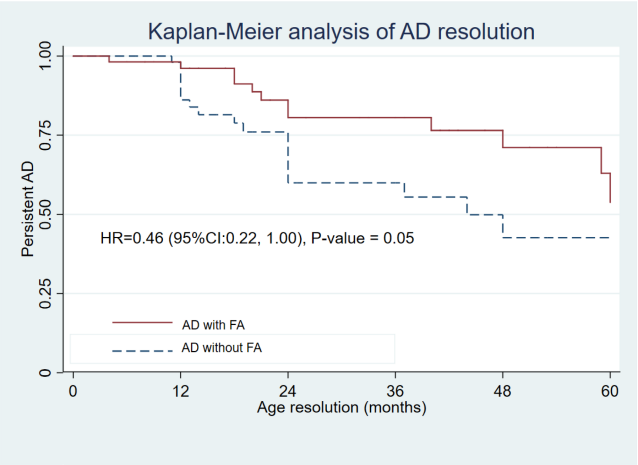
Background: Atopic dermatitis (AD) is a chronically relapsing inflammatory dermatosis and characterized by dry and pruritic skin. Food allergy (FA) is often reported in one-third of AD children, particularly in moderate to severe AD. Although, the dual-allergen exposure hypothesis has been postulated, multifactorial etiology might play an important role and involving in this complex disease.

Method: A questionnaire-based observational study was conducted in Allergy and Dermatology clinic, Department of Pediatrics, Siriraj Hospital Mahidol University, Bangkok, Thailand. All patients age less than 6 years who were physician diagnosed with AD by Hanifin and Rajka criteria were included in this study. The diagnosis of FA was made by Pediatric Allergists. Potential factors were analyzed using multivariable logistic regression and the age of AD resolution was analyzed using Kaplan-Meier estimates.

Results: A total of 110 children were enrolled (67 male, median age of 2.3y (range 1.2–3.8)). Of which, 57 of them had AD without FA, and 53 children had AD with FA (30.2% with single FA, and 69.8% with multiple FA). Very early onset of AD (<3mo), and moderate to severe AD at the onset were reported in 43.9%, and 26.3% in AD without FA, and 35.8%, and 45.4% in AD with FA, respectively. The most common reported FA were hen's egg (67.9%), followed by cow's milk (60.4%), wheat (58.5%), soybean (24.5%), fish (22.6%), shellfish (15.1%), and peanut (11.3%). Moderate to severe AD at onset was found to be a significant risk factor associated with FA (adjusted odd ratio 2.52; 95%CI: 1.05–6.03, p = 0.038), after adjusting for all potential risk factors. Thirty-one patients (28.1%) resolved from AD at, 8.2% resolved at 1-year, 21.8% at 2-year, and 28.1% by 6-year of age. Among children resolved from AD, 19(33%) were from AD without FA, and 12(22.6%) were from AD with FA, with the median age of AD resolution at 1.5y (IQR 1,2), and 1.6y (IQR 1.5,1.8), respectively. AD children with FA had a trend toward slower rate of remission as compared to AD children without FA, after adjusting for onset and severity of AD (adjusted hazard ratio 0.46; 95%CI: 0.22–0.99, p = 0.05).

Conclusion: In preschool AD children with FA, the severity of AD at onset was greater, and resolution age of AD tended to be later as compared to AD children without FA.



Conflicts of interest: The authors did not specify any links of interest.

000088 | Home-based introduction of egg protein in paediatric IGE-mediated egg allergy – A review of treatment strategy 2011–2021

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Background: Egg allergy is the second most common food allergy in children and one of the main causes of anaphylaxis in infants. In many European countries standard practice for children with IgE-mediated egg allergy is total avoidance until 6–7 years old. However, recent studies have shown that the early stepwise introduction of egg to the diet can promote earlier tolerance. In Ireland reintroduction of egg to the diet is reached following home-based induction of egg protein via the egg ladder. Seemingly the longer the egg allergy persists the less likely the child will achieve tolerance; therefore early introduction is imperative.
Method: A sample of 300 charts of children treated for IgE-mediated egg allergy in the paediatric clinic in Cork University hospital from 2011 to 2021 were reviewed. Inclusion and exclusion were applied. Data were analysed using STATA.
Results: 300 charts reviewed, 78 excluded due to Skin Prick Test (SPT) <3mm and 23 excluded due to incomplete documentation. 22 lost to follow-up, 24 still ongoing treatment, 2 discontinued treatment due to malignancy diagnosis, 18 did not achieve tolerance and were still avoiding egg in some form. This resulted in 133 children who completed the egg ladder and were included in statistical analysis ($N = 133$). Mean time to complete ladder and achieve tolerance was 30 months. Concomitant peanut allergy increased time to achieve tolerance by 10.63 months and documented parental anxiety resulted in 11.26 months longer on the egg ladder. For each unit increase in Specific IgE (kIU/L) time to achieve tolerance was increased by 0.2 months. Other variables were included in the construction of the model however, were not significant and reduced the R^2 and were removed from the final regression. 40 had symptoms of anaphylaxis at time of diagnosis. Only 1 had anaphylaxis while on the egg ladder, due to accidental exposure.
Conclusion: Home based introduction of egg protein via the egg ladder is safe and effective. Specific IgE, history of peanut allergy and parental anxiety are useful predictors of duration of treatment.
Conflicts of interest: The authors did not specify any links of interest.

000429 | Prognostic factors facilitating multiple food allergies and atopic march occurrence in children with non-IGE-mediated gastrointestinal food allergy: Results of two years follow up of the NIGEFA project

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*Presenting author: L. Carucci

Background: Many aspects of non-IgE mediated gastrointestinal food allergies (non-IgE-GIFA) (including four phenotypes of food protein-induced enterocolitis syndrome, FPIES; enteropathy, FPE; allergic proctocolitis, FPIAP; and motility disorders, FPIMD), are still poorly characterized. The NIGEFA project was launched for the investigation of these conditions.
Method: Prospective observational study evaluating children with non-IgE-GIFA diagnosed according to standard criteria observed at a tertiary center for pediatric gastroenterology and allergy (both sex, aged <14 y, follow up 24 m). Main anamnestic and clinical data were collected from all enrolled patients.
Results: 123 children (56% male) with a median (IQR) age of 150 (60–300) days were enrolled into the study. The frequency of non-IgE-GIFA was: FPE (39%), FPIES (17%), FPIAP (16%), and FPIMD (28%). 42% of children had multiple food allergies (FA) at baseline and 64% had a family risk for allergy. Male sex (Odds Ratio (OR) = 2.24, 95%CI 1.07 to 4.71) and 1-month diagnostic delay (OR = 1.09, 1.01 to 1.18) were associated with multiple FA. The 24-mo overall rate of immune tolerance acquisition was 54%, with a higher rate in FPIAP (75%) compared with FPIMD (62%), FPE (54%) and FPIES (24%). The odds of 24 m immune tolerance acquisition rate were lower in children with family risk for allergy (OR = 0.41, 0.19 to 0.89) and in those with multiple FA at baseline (OR = 0.24, 0.11 to 0.51). At the 24m follow up, the atopic march was observed in 46% patients, with similar rates in the four clinical phenotypes. The presence of multiple FA at baseline was associated with atopic march occurrence (OR = 2.22, 1.07 to 4.61) at 24 months.
Conclusion: These data suggest the importance of early diagnosis to prevent the occurrence of multiple FA and of the atopic march and to hasten the immune tolerance acquisition in children with non-IgE-GIFA.
Conflicts of interest: The authors did not specify any links of interest.

000550 | The allergenicity ladder: A possible approach for home-base fish introduction in children with IGE-mediated fish allergy?

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Background: Fish is a valuable source of healthy nutrients with increasing global demand. Fish allergy affects 0.1%–0.4% of the world's population, has an early onset and tends to persist throughout life. With the high sequence and structural homology of parvalbumins, the major fish allergen, allergy to multiple fishes is common. However, there are reports of mono-allergy to single fish but tolerating others, thus suggesting allergenicity differences in edible fishes. We therefore hypothesize that commonly consumed fish present different allergenicity (ladder) leading to different clinical presentation of fish allergy, and the identification of the allergenicity ladder allows gradual and safe home re-introduction of fishes in children with IgE-mediated fish allergy. This study thus aimed at distinguishing the IgE reactivity of commonly consumed fish for the construction of such ladder.

Method: Physician-diagnosed fish allergic subjects (n = 200) were recruited from five regional hospitals in Hong Kong. IgE reactivity against three freshwater fishes (tilapia, grass carp and catfish), six marine fishes (cod, salmon, tuna, grouper, herring and halibut) and two recombinant parvalbumins (rCyp c 1 and rGad c 1) was measured by ImmunoCAP Specific IgE (sIgE) assays.

Results: With a cut-off value of 0.35 kUA/L, 166 subjects were positive to at least one of the assays tested. The major causative fish among these sensitized subjects was grass carp (44%) while the leading tolerant fish was salmon (27%). One-third of the sensitized subjects had negative sIgE level (class 0) to tuna, halibut and salmon, while the pattern reversed with one-third of these subjects presenting high sIgE levels to the freshwater fishes (classes 4–6). A significant positive correlation was detected between self-reported reaction and sIgE level to the corresponding fish (Pearson r = 0.809, p = 0.0151), while the level of sIgE was not related to the frequency of consumption (r = −0.214, p = 0.6112).

Conclusion: Based on sIgE reactivity, common edible fishes can be grouped as low (tuna, halibut and salmon), moderate (cod, herring and grouper), and high (catfish, grass carp and tilapia) allergenicity fish. Such ladder potentially provides possible strategies for reducing the number of sIgE test and for safe and gradual home re-introduction of fishes by gradually "stepping up the ladder".

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Conflicts of interest: The authors did not specify any links of interest.

000138 | The influence of breastfeeding on the occurrence of IGE-mediated food allergy

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*Presenting author: I. Lachover-Roth

Background: IgE-mediated food allergy is a growing health problem affecting up to 10% of the children. It is well established that early introduction of peanuts and eggs since 4 months of age has a preventive effect. However, there are infants that are already sensitized at that age. The leading theory for the early sensitization is exposure through the skin, especially in atopic infants. The Cow's Milk Early Exposure Trial (COMEET) study showed that continuous exposure to cow's milk formula (CMF) since birth has a preventive effect on the development of cow's milk allergy.

The current study assesses the effect of breastfeeding versus CMF feeding on the development of IgE-mediated food allergy.

Method: 1989 infants of the COMEET study were divided into three groups for the first two months of life, according to parents' feeding preference: Group 1: exclusive breastfeeding (EBF); Group 2: breastfeeding with at least one daily meal of CMF and Group 3: feeding with CMF only. All were followed with monthly questioner until the age of 12 months. When the history suggested immediate allergic reaction to food product, diagnosis was confirmed by skin test.

Results: From the total of 1989 infants, 1071 were EBF (53.8%), 616 were breastfed with addition of CMF (31%), and 302 were fed by CMF only since birth (15.2%). A total of 43 infants developed IgE-mediated food allergy (cow's milk, egg, peanut, sesame, tree nuts, almonds, and soy) (2.2%); 31 in the EBF group (2.9%), 12 in the group fed by combination of breastfeeding and CMF (1.9%), and zero in the CMF feeding only group (p = 0.002). Family atopic comorbidity did not influence the results.

Conclusion: Breastfed infants, either exclusivly or in combination with CMF, seems to develop significantly more IgE-mediated food allergy during the first year of life. One may speculate that the mechanism is related to compounds injested by the mother and secreted in the breastmilk. Irregular or incidental exposure of the mother can cause sensitization rather than tolerance. A larger cohort is needed in order to validate these results.

Conflicts of interest: The authors did not specify any links of interest.

000781 | Walnut allergy starts with high risk of anaphylaxis around toddler age: A multi-center cross-sectional study with 366 subjects

S. Ishibashi[1]; A. Kawai[1]; T. Itonaga[1]; Y. Miura[1]; N. Yanagida[1]; S. Sato[1]; E. Makita[2]; H. Taniguchi[3]; T. Kitatsu[4,5]; Y. Koike[6]; M. Ebisawa[1]

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*Presenting author: S. Ishibashi

Background: Tree nut is a common allergen in Westernized countries and often causes anaphylaxis. In addition, tree nut allergy is becoming increasingly prevalent in Japan, led by walnut allergy. In this study, we aimed to describe the clinical features of the onset of walnut allergy in the Japanese pediatric population.

Method: We conducted a multi-center cross-sectional study and retrospectively collected clinical data of children with walnut allergy from medical charts. Patients aged 0 to 15 who visited the participating institutions between 2013 and 2022, with a clear history of immediate reaction with walnut ingestion and confirmed walnut sensitization on blood tests were included. Information on the patient's initial reaction with walnut ingestion, background, allergic comorbidities, and serological data were obtained. The primary outcome was the age of the initial reaction.

Results: A total of 366 patients were included in this study. The median age of the initial reaction was 42 months (interquartile range: 30–61 months). The median values of specific IgE to walnut and Jug r 1 within a year of the initial reaction were 10.5 kU_A/L (interquartile range: 4.0–26.2 kU_A/L) and 7.1 kU_A/L (interquartile range: 3.0–21.0 kU_A/L), respectively. The rate of infantile eczema, atopic dermatitis, bronchial asthma or recurrent wheeze, and allergic rhinitis were 69% (246/359), 59% (212/361), 27% (96/361), and 35% (118/334), respectively. History of immediate reaction to other foods prior to walnut was seen in 57% of the patients, and the most common causative foods were egg, milk, peanut, wheat, and cashew nut. Sensitization to walnut was confirmed before the initial reaction in 12% of the patients, and the initial reaction occurred during oral food challenge (OFC) in 7% of the patients. During the initial reaction, cutaneous, mucous, gastrointestinal, respiratory, and cardiovascular symptoms were seen in 76%, 43%, 37%, 37%, and 8% of the patients, respectively. Anaphylaxis occurred in 31% of all initial reactions and in 13% of initial reactions during OFCs.

Conclusion: In Japanese children with walnut allergy, the initial reaction occurred most during preschool years, and anaphylaxis was common. Further investigation is required to develop a method to identify children at high risk of walnut allergy.

Conflicts of interest: The authors did not specify any links of interest.

000894 | Timing of allergenic food introduction and risk of IGE-mediated food allergy: Systematic review and meta-analysis

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*Presenting author: R. Scarpone

Background: Earlier egg and peanut introduction probably reduce risk of egg or peanut allergy, but it is uncertain whether food allergy as a whole can be prevented using earlier allergenic food introduction. This study is a systematic review on timing of allergenic food introduction to the infant diet and risk of food allergy.

Method: Medline, Embase and CENTRAL were searched to December 2022. Randomized controlled trials evaluating timing of allergenic food introduction during infancy were included. Data were extracted in duplicate and synthesized using a random-effects model. GRADE was used to assess certainty of evidence. Primary outcomes were risk of allergy to any food and withdrawal from the intervention. Secondary outcomes included allergy to specific foods.

Results: Of 9283 titles screened, data were extracted from 23 eligible trials (56 reports; 13749 randomized participants). There was moderate-certainty evidence from 4 trials (3295 participants) that earlier introduction of multiple allergenic foods at 2 to 12 months (median 3 to 4 months) was associated with reduced food allergy (RR, 0.49; 95% CI, 0.33–0.74; I^2 = 49%). Absolute risk reduction for a population with 5% incidence of food allergy was 26 cases (95% CI, 13–34 cases) per 1000 population. There was moderate-certainty evidence from 5 trials (4703 participants) that earlier introduction of multiple allergenic foods at 2–12 months was associated with increased withdrawal from the intervention (RR, 2.29; 95% CI, 1.45–3.63; I^2 = 89%). Absolute risk difference for a population with 20% withdrawal from the intervention was 258 cases (95% CI, 90–526 cases) per 1000 population. There was high-certainty evidence from 9 trials (4811 participants) that earlier introduction of egg at 3 to 6 months was associated with reduced egg allergy (RR, 0.60; 95% CI, 0.46–0.77; I^2 = 0%); and high-certainty evidence from 4 trials (3796 participants) that earlier introduction of peanut at 3 to 10 months was associated with reduced peanut allergy (RR, 0.31; 95% CI, 0.19–0.51; I^2 = 21%). Evidence for timing of introduction of cow's milk and risk of milk allergy was very low certainty.

Conclusion: Earlier introduction of multiple allergenic foods was associated with lower risk of developing food allergy, but a high rate of withdrawal from the intervention.

Conflicts of interest: Dr Boyle reports editorial fees from Cochrane and Wiley and expert witness fees from Taus, Cebulash and Landau.

000566 | Follow up after baked milk introduction in cow milk allergic children

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Background: Based on cohort and retrospective studies, several authors suggested that the introduction of baked milk (BM) products into the diet may speed the resolution of milk allergies along with positive effects on quality of life and nutrition. Only recently, a controlled randomized clinical trial has been published showing that introducing BM in cow milk allergy (CMA) patients accelerates the tolerance to fresh milk (FM).

The goal of this real study is to describe the clinical and immunological evolution of the CMA patients who introduce BM into their diet after a negative challenge test.

Method: We have performed a retrospective real-life study of CMA patients, with at least one year of follow up, since the moment we confirmed BM tolerance and their introduction of BM products regularly, until the day they tolerate FM in the challenge test or until present time. We collected clinical data and specific IgE levels at different times during the follow up.

Results: Thirty-eight patients were included, the median age to achieve BM tolerance was 35 months. All patients tolerated BM at home without reactions. The adherence was 95%, only two patients stopped the BM introduction. 61.11% had a negative FM challenge test, the average time required to tolerate FM was 18 months. 19.44% had a positive FM challenge test. 19.45% have not undergone a FM challenge test yet. The value of specific IgE for milk protein decreased in 84% of the cases, being statistically significant. In the rest of the cow milk fractions a decrease was observed (64%–72% of patients), without reaching a statistical significance.

Conclusion: The introduction of BM in our children population was safe and the majority of the patients became tolerant to FM in 12–24 months, with a decrease in cow milk IgE specific values.

This is a real life study that reinforces the idea that early introduction of BM benefits CMA patients.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on food allergy treatment

000191 | The harmony trial: Baseline characteristics from a phase 1/2 trial of ADP101 for oral immunotherapy in children and adults with single or multiple food allergies

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*Presenting author: S. Gogate

Background: Use of single-allergen oral immunotherapy (OIT) in patients with food allergies is limited by the need for multiple products and the time spent in sequential rounds of therapy for those with multiple allergies. Enhanced treatment options for these patients are needed. ADP101 is a multiallergen OIT in development to treat allergy spanning the 9 major food allergen groups. ADP101 is a mixture of equal parts by protein weight of allergenic proteins from 15 foods (ie, almond, cashew, chicken's egg, codfish, cow's milk, hazelnut, peanut, pecan, pistachio, salmon, sesame, shrimp, soy, walnut, wheat). The Phase 1/2 Harmony trial (NCT04856865) is a randomized, double blind, placebo-controlled trial currently underway to evaluate the efficacy and safety of ADP101 for inducing desensitization in patients with single or multiple food allergies.

Method: Eligible patients were aged 4 to 55 years and had a qualifying food allergy to 1–5 foods contained in ADP101, defined as dose-limiting symptoms on exposure to ≤100 mg on double-blind, placebo-controlled food challenge (DBPCFC) at screening. Nonqualifying foods were those eliciting a reaction at >100 mg but ≤1000 mg on DBPCFC. Patients were randomized to either a low-dose (1500 mg/day) or high-dose (4500 mg/day) regimen of either ADP101 or matched placebo, which included an initial up-dosing phase followed by a maintenance phase. The primary efficacy measure is the response rate, which is defined as the proportion of patients who tolerate ≥600 mg of ≥1 qualifying food without dose-limiting symptoms on exit DBPCFC. Exploratory analyses will evaluate whether allergy to nonqualifying foods responds to treatment with ADP101.

Results: A total of 109 patients were screened across 16 US clinical sites, and 73 patients with single or multiple food allergies were enrolled between April-December 2021. Most participants were children (per protocol), had multiple food allergies, and had a history of anaphylaxis (**Table**). All 15 targeted allergens contained in ADP101 are represented as qualifying food allergies in the study cohort. Eliciting doses ranged from 1 to 100 mg, and aggregated nonpeanut allergens presented with slightly lower eliciting doses than peanut allergen (**Figure**). About one-third of patients had nonqualifying food allergy.

Conclusion: The Harmony trial will evaluate the potential of ADP101 as a multiallergen OIT to simultaneously treat patients with one or more food allergies.

Baseline characteristics	All participants (N=73)
Sex	
Male	44 (60%)
Female	29 (40%)
Age group	
Pediatric (4-17 years old)	61 (84%)
Adult (18-55 years old)	12 (16%)
Race	
White	52 (71%)
Black	3 (4%)
Asian	13 (18%)
Other	5 (7%)
Number of food allergies (qualifying and nonqualifying)	
Single	25 (34%)
Multiple	48 (66%)
Number of qualifying food allergies	
1	38[a] (52%)
2	14 (19%)
3	11 (15%)
4	5 (7%)
5	5 (7%)
Prior history of anaphylaxis	51 (70%) (83% of adults; 67% of children)

Data shown as n (%).
[a]25 patients had a single qualifying allergy and 13 had a single qualifying allergy and ≥1 nonqualifying allergies. Qualifying food allergy defined as dose-limiting symptoms on exposure to ≤100 mg protein on double-blind, placebo-controlled food challenge (DBPCFC) at screening; nonqualifying food allergy defined as dose-limiting symptoms on exposure to >100 mg but ≤1000 mg protein on screening DBPCFC.

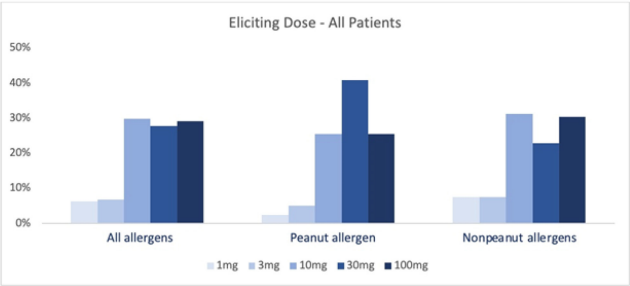

Figure legend. Eliciting dose in the Harmony trial for qualifying food allergies, defined as the allergen dose that elicits dose-limiting symptoms during DBPCFC.

Conflicts of interest: M-L Wang, A. Sullivan, N. Rabbee, A. Dombkowski, D. McClintock are employees of Alladapt ImmunotherapeuticsS. Gogate has advised for Novartis and IgGenix.

001374 | Can altering the early life environment protect children with a FLG null mutation from developing food allergy?

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Background: Filaggrin gene (*FLG*) null mutations contribute to poor skin barrier and are associated with increased risk of food allergy. It is unclear whether risk of food allergy conferred by a *FLG* null mutations can be attenuated by potentially modifiable factors. Knowledge of such factors can inform intervention strategies. We assessed whether breastfeeding duration, timing of solids introduction and microbial exposure (pet exposure and presence of older siblings) modified the association between *FLG* and food allergy.

Method: In the population-based HealthNuts study, 5276 infants aged 1 year were screened for possible food allergy by skin prick testing (SPT). Infants with SPT ≥1mm proceeded to oral food challenge (OFC). Additionally, 200 infants with 0mm SPT had OFC. At age 6 years, those with challenge-confirmed food allergy at 1 year were offered SPT and OFC to test for persistence of food allergy. This sub-study included Caucasian infants who attended the OFC clinic at age 1 year and gave blood samples which were genotyped for five common FLG mutations in Caucasian populations, (n = 423); infants who were food sensitised (SPT ≥2mm) but tolerant were excluded. Associations between FLG null mutations and food allergy were analysed using logistic regression and likelihood ratio tests were used to assess interactions.

Results: *FLG* null mutations were associated with food allergy at both 1 (aOR 4.49 95%CI 1.33–9.12) and 6 years (aOR 3.18, 95%CI 1.10–9.19). Presence of a *FLG* null mutation was not strongly associated with food allergy at age 1 in children who were breastfed for ≥12 months, (aOR 1.23, 95%CI 0.39–4.61), while breastfeeding for a shorter period (<12 months) was associated with a higher risk (aOR 15.63, 95%CI 2.66–+∞). This pattern was also seen for food allergy at age 6 years. Presence *FLG* null mutation appeared to somewhat increased risk of food allergy at age one if they did not have a cat (aOR 2.35, 95%CI 0.86–8.06), but this association was stronger when infants were exposed to pet cats (aOR 9.08, 95%CI 1.36–+∞). There was little evidence of effect modification by exposure to pet dogs, older siblings, exclusive breastfeeding or timing of solid food introduction.

Conclusion: These results suggest that the risk of food allergy conferred by a *FLG* null mutations is potentially modifiable by breastfeeding for longer 12 months or avoiding exposure to cats in infancy. Further studies are needed to explore mechanisms and replicate these findings.

Conflicts of interest: MLKT has received research funding from Prota Therapeutics, is an employee of Prota Therapeutics, has received consultancy fees from Pfizer and is an inventor on patents owned by MCRI "A method for of inducing tolerance to an allergen" and "Allergy Treatment". KPP is Chair of the scientific advisory board for AllergyPal; her institution has received research grants from DBV Technologies, Novartis and Siolta and consultant fees from Aravax; outside the submitted work SCD and AJL received investigator-initiated grants from GSK for unrelated work. AJL, SCD and JJK have received grant funding from Sanofi Regeneron for unrelated research. AJL has received in kind contributions of study intervention (EpiCeram) from Primus Pharmaceuticals for unrelated research. RP receives honoraria for editorial involvement with the journal Paediatric Allergy and Immunology. All other authors have no COI to declare.

000961 | Efficacy and safety of oral immunotherapy for peanut allergy in children aged 1 to

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Background: Oral immunotherapy with defatted powder of *Arachis hypogaea* L., semen (peanuts) (PDAH) has demonstrated efficacy and safety in multiple phase 3 trials and is approved in Europe and the United States for the treatment of patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy. The POSEIDON trial (NCT03736447) assessed the efficacy and safety of PDAH in younger children with peanut allergy.

Method: POSEIDON was a global, double-blind, placebo-controlled, randomised phase 3 trial involving children with peanut allergy aged 1 to <4 years. Children who developed dose-limiting symptoms after ingesting single doses of peanut protein >3 mg to ≤300 mg during a screening double-blind, placebo-controlled food challenge (DBPCFC) were randomised 2:1 to daily PDAH or placebo. Participants were treated for a total of ~12 months. The primary efficacy endpoint was the proportion of participants tolerating a single ≥1000 mg dose of peanut protein during the exit DBPCFC. Secondary endpoints included symptom severity and tolerability at other peanut protein doses during exit DBPCFC. All treatment-emergent adverse events (AEs) were recorded.

Results: Of 146 children receiving treatment (PDAH, n = 98; placebo, n = 48), 68.4% of individuals receiving PDAH tolerated a single dose of 1000 mg peanut protein (2043 mg cumulative; vs 4.2% for placebo) at exit DBPCFC (difference, 64.2%; 95% CI, 47.0%–81.4%; $p < 0.0001$). A total of 61.2% of PDAH-treated patients tolerated the highest dose level assessed of 2000 mg (4043 mg cumulative) vs 2.1% for placebo (difference, 59.1%; 95% CI, 42.1%–76.2%; $p < 0.0001$). A total of 6 individuals (6.1%) in the PDAH group discontinued due to any AE (the majority during up-dosing) vs zero patients in the placebo group. Treatment-related adverse events (TRAEs) were reported by 75.5% of PDAH-treated patients vs 58.3% for placebo. All TRAEs were mild-to-moderate with no serious or severe TRAEs reported.

Conclusion: Treatment of peanut allergy with PDAH in children aged 1 to <4 years demonstrated a favourable safety profile and resulted in clinically relevant peanut desensitisation with the majority of PDAH-treated participants tolerating a maximum single dose of 2000 mg of peanut protein (4043 mg cumulative) during exit DBPCFC.

Conflicts of interest: S.T., K. B. and A. V. are employees of Aimmune Therapeutics.

000544 | Treating peanut allergy with an IGG4 monoclonal antibody-based approach

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Background: Peanut allergy is an increasingly prevalent unmet medical need that affects children and adults worldwide. The standard of care, allergen avoidance and rescue epinephrine administration, is unsatisfactory to patients and caregivers, and while advancements have been made in desensitization approaches such as oral immunotherapy, patients often suffer from frequent adverse events and face extended time horizons to treatment outcomes. Consequently, there remains a need for a safe and efficacious therapeutic with a rapid onset of action that protects against accidental allergen exposure and improves quality of life.

Method: IgGenix isolated rare IgE antibodies from peanut allergic individuals using its proprietary single-cell RNA-sequencing discovery platform technology. IgE antibodies were then re-engineered as monoclonal IgG4 antibodies and assayed for their allergen specificity, affinity, and binding epitopes. Promising candidates were advanced through lead evaluation involving *in vitro* plasma IgE blocking ELISAs, mast cell activation tests, *ex vivo* basophil activation tests, *in vivo* animal models, and developability assessments.

Results: Antibodies discovered in an unbiased manner from numerous peanut allergic individuals preferentially bound Ara h 2 and/or Ara h 6, with a minority of antibodies binding other allergens. Antibodies specific to Ara h 2 and Ara h 6 distributed nonuniformly into a small number of epitope bins, revealing immunodominance of specific epitopes on each allergen. Nearly all antibodies were of high affinity, with many exhibiting double-digit picomolar affinity. Select antibodies, when engineered and combined, were able to inhibit allergic plasma IgE from binding recombinant Ara h 2, inhibit peanut-mediated mast cell and basophil activation, and prevent anaphylaxis mediated by oral peanut challenge in a mouse model of peanut allergy.

Conclusion: An unbiased human IgE discovery platform based on single-cell RNA-sequencing is a powerful foundation from which to generate high affinity IgG4 antibodies that bind to immunodominant allergens and immunodominant epitopes on those allergens. These IgG4 monoclonal antibodies can form the basis of a therapeutic candidate exhibiting strong potency and efficacy *in vitro*, *ex vivo*, and *in vivo*. This enables a new paradigm for food allergy treatment characterized by protection within days of subcutaneous administration and the absence of adverse events associated with allergen administration.

Conflicts of interest: **All authors are are employees of, and/or stakeholders in, IgGenix, Inc.**

001096 | Hazelnut cross desensitization following walnut oral immunotherapy

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Background: We have previously shown that 8/15 walnut-hazelnut co-allergic patients are fully cross-desensitized to hazelnut following successful walnut oral immunotherapy (OIT). We aimed to examine these findings in a large group of patients

Method: Walnut-hazelnut co-allergic patients who began walnut OIT, with a goal of full desensitization to 4000 mg protein, between July-2016 and July-2021 were analyzed. Walnut and hazelnut allergy were diagnosed based on an oral food challenge or a recent reaction. All patients underwent walnut OIT and were subsequently challenged to hazelnut again

Results: A total of 82 walnut-hazelnut co-allergic patients began walnut OIT during the study period, and 77 (93.9%) were fully desensitized. Additional 4 patients were desensitized to 1200 mg protein and a single patient failed. Of those fully desensitized, 69 patients (92%) were challenged to hazelnut following OIT. Fifty-five of those patients were challenged to hazelnut before walnut OIT with a median reaction dose of 150 mg (range, 5–2400 mg) and the remaining 14 patients were diagnosed based on a recent reaction to hazelnut. Forty-six patients (66.7%) were fully desensitized to hazelnut following walnut OIT. Additional 6 patients reacted to >1000 mg hazelnut protein and the remaining 17 patients reacted to <1000 mg hazelnut protein following walnut OIT. Patients wo were cross-desensitized to hazelnut following walnut OIT had a lower median (IQR) hazelnut SPT (8 mm, 6–10 vs. 9.5 mm, 8–13.2, p = 0.045) and a higher median hazelnut reaction dose (263 mg, 120–1890 vs. 60 mm, 20–300, p = 0.005) before walnut OIT, and a lower median hazelnut SPT (6 mm, 5–7 vs. 8 mm, 6–9.5, p = 0.006) after walnut OIT compared to those who remained hazelnut allergic.

Conclusion: Walnut OIT induces cross-desensitization in most hazelnut co-allergic patients, particularly those with less severe hazelnut allergy at baseline. Most patients with walnut-hazelnut co-allergy would benefit from a single walnut treatment which would minimize their load of long-term consumption.

Conflicts of interest: The authors did not specify any links of interest.

000963 | Beneficial effects of sublingual immunotherapy with PRU P 3 and dietary supplementation with butyrate in an anaphylactic mouse model

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Background: Food Allergy (FA) is as an immunological adverse reaction triggered after the ingestion of certain foods. From plant-food allergens, Pru p 3, which is a non-specific lipid transfer protein (nsLTP), is frequently involved in FA and causes severe reactions. Allergen immunotherapy (AIT) with the allergenic protein is a promising treatment. Previous studies demonstrated the effectiveness of Pru p 3 sublingual immunotherapy (SLIT) in nsLTP-allergic patients; however, there are no studies about the effect of administering other dietary components, such as dietary fibre or short-chain fatty acids like butyrate. Thus, we aim to study the effects of including pectin and butyrate as dietary supplement in the treatment of allergic mice with Pru p 3-SLIT.

Method: Female Balb/c mice were intranasally sensitised for 5 weeks with 20 µg Pru p 3 plus 10 ng LPS and divided into six groups (n = 7): 1) Sensitised, Non-treated; 2) Sensitised, Pru p 3-SLIT; 3) Sensitised, Pectin; 4) Sensitised, Pectin + Pru p 3 SLIT; Sensitised, Butyrate; 6) Sensitised, Butyrate + Pru p 3 SLIT. After 8 weeks of SLIT, mice were intraperitoneally challenged with 50 µg of Pru p 3. Body temperature and clinical symptoms were annotated, and maxillary and mesenteric lymph nodes (LNs) and spleen were collected and processed. Several co-stimulatory molecules from dendritic cells (DCs) and proliferative responses of lymphocyte subpopulations from spleen were evaluated by flow cytometry.

Results: Mice treated with SLIT-Pru p 3, pectin and/or butyrate were partially protected from anaphylaxis after challenge. Although they showed a drop in body temperature, lower levels of clinical score were observed in these groups in comparison to untreated mice. Maxillary-DCs and mesenteric-DCs seem to show a different profile of co-stimulatory molecules. After stimulation with Pru p 3, maxillary-DCs of all treated groups reduced the CD80 and CD86 levels, whereas mesenteric-DCs had a significant decrease in CD83 marker. Moreover, mice treated with butyrate plus Pru p 3 exhibited an increase in IFN-γ^+ and IL-10^+ DCs levels. Finally, regulatory T cells percentage was higher in mice treated with a butyrate supplementation than in the rest of groups.

Conclusion: SLIT with Pru p 3 and dietary supplementation with butyrate represent a good therapeutic option for FA by inducing protection against anaphylaxis and immunological changes towards a tolerance profile.

Conflicts of interest: The authors did not specify any links of interest.

001269 | Is there a public interest on the internet about food allergies? An infodemiology analysis

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*Presenting author: I. Cherrez-Ojeda

Background: Food allergies affect 10% of the global population and have a significant impact on quality of life. The global public's interest in food allergies is growing, and the internet, which has 63.1% global penetration, is the primary source of information. The Internet is an appealing source of information due to its ease of access and readily available information; however, not all of this information is of high quality or evidence-based. In this regard, the aim of our study is to describe what people are searching for when they think of food allergies, what terms they use, and which countries have the most interest.

Method: This is a Cross-Sectional study using 1) Google trends tool to search Seafood, Peanuts, and Milk as main topics in ten countries (Australia, Canada, Finland, Hungary, Ireland, Netherlands, New Zealand, Philippines, Singapore, USA) from 2012 to 2021; 2) a qualitative analysis of the main related terms, and 3) Forecasting models using the Autoregressive Integrated Moving Average (ARIMA) model. The data was obtained on Sept 25, 2022.

Results: Over 400 entities related to each food allergy were gathered. Milk allergy was the most searched term in all 10 countries, followed by peanut allergy. Pharmacological and non-pharmacological strategies were also searched including epinephrine in Singapore and milk substitutes (such as almond milk). For seafood and peanut allergies, people had a higher interest in symptoms. By 2023, we forecasted a significant increase in food allergy-related searches in Australia, the Philippines, and Singapore.

Conclusion: Our findings showed individuals have a greater interest in searching for milk allergy compared to other types of allergens, even though it is not the most prevalent. These results aim to collect information about the trends people exhibit when searching for food allergies, regardless of whether they have the condition or not, these results provide a foundation for future patient education tools that can empower affected individuals to engage in self-management and achieve better outcomes for their condition.

Conflicts of interest: The authors did not specify any links of interest.

000529 | Comparisons of cashew, pistachio, walnut, and peanut vicilin-buried peptide allergens

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*Presenting author: G. Mueller

Background: Vicilin-buried peptides (VBPs) are derived from the N-terminal leader-sequence (LS) of vicilin proteins and are receiving increasing attention as a novel class of food allergens. Characterizing the VBPs from peanuts and tree nuts may help understand comorbidity and cross-reactivity among tree nuts and legumes despite a distant evolutionary origin.

Method: Peptide microarrays were used to identify IgE-reactive sequences from the LS of the vicilin allergens from Ara h 1, Ana o 1, Jug r 2, and Pis v 3 using serum from patients diagnosed as peanut and/or walnut/pistachio/cashew allergic. The structure of four VBPs were solved using solution-NMR (cashew: AO1.1, AO1.2 and pistachio: PV3.1, PV3.2), and compared to solved VBP structures from peanut (AH1.1) and walnut (JR2.1, JR2.2, and JR2.3). Biophysical properties were assessed using in vitro proteolysis assays and circular dichroism. Hybridomas of B-cells from allergic patients were screened for cells producing IgE against VBPs.

Results: IgE binding to peptides was frequently observed in the VBP domains AH1.1, AO1.1, JR2.1, and PV3.1, and not in AO1.2, JR2.2, JR2.3, PV3.2. Comparisons of structural features suggest the VBP scaffold can support cross-reactivity despite low sequence identity. The cashew VBPs are more resistant to proteolysis than the pistachio VBPs, correlating with a slight increase in prevalence. Human IgE monoclonal antibodies were discovered with specificity for AH1.1 and JR2.1.

Conclusion: VBPs are domains derived from vicilin allergens with variable IgE-binding prevalence in microarray data, ranging from near 100% of patient sera IgE binding (JR2.1) to less than 10%. The conserved VBP fold could allow for cross-reactivity with peanuts and tree-nuts including walnut. However, thus far, human IgE, secreting B-cells were found with high specificity exclusively for JR2.1 or AH1.1. Further research is needed to correlate the VBP IgE levels to clinical reactivity cross-reactivity.

Conflicts of interest: The authors did not specify any links of interest.

001666 | Cow milk allergy after an elimination diet, in a previously tolerant child

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CASE REPORT

Background: Food allergy (FA) and atopic dermatitis (AD) coexist in many children, with FA considered one of AD potential triggers. Although in the forefront for decades, elimination diets are now believed to carry more risks than benefits in management of AD. We opt to bring evidence that the removal of a previously consumed food in children with AD can result in food allergy upon reintroduction.

Case Report: Our patient is a 4 years old girl who has AD since infancy. At age of 7 months she had a persistent AD deterioration, and parents decided to have specific IgE measurement for most common food allergens. She had started solids and an age appropriate formula the last month, without appearance of any allergy symptoms. Despite this, the mother and her baby initiated a very restricted elimination diet, on advice from a health care provider, based on specific IgE levels resulting in multiple sensitizations to food. After elimination the AD had not improved, but nevertheless they continued the diet for several months.

The child came to our hospital at the age of 14 months, with growth failure and a severe atopic dermatitis. In the next months, after skin test and some food challenges, several foods were introduced successfully in the child's diet. Her AD condition improved gradually, with intense moisturizing treatment and on demand topical corticosteroids. The parents refused oral food challenge for cow milk and hypoallergenic formulas, because of persistent positivity in skin prick test. After one year on amino acid-based formula and soya products, the girl came in our hospital for reevaluation of milk allergy. Skin prick test to cow milk resulted in an increased reaction, from 5mm at 1.5 years old to 14mm at around 3 years old. The last year, the girl had some local reactions with urticaria and facial oedema in 2 occasions, after being kissed from her parents, who had consumed milk before.

Conclusions: There is a complex association between FA and AD, with evidence supporting that AD plays a role in the food allergy acquisition and not vice versa. Furthermore, elimination diets in children with multiple sensitizations to foods, have been associated with negative impacts ranging from nutritional risks, and subsequent growth failure to IgE-mediated food allergy. Health care providers should consider these risks before recommending elimination diet of well tolerated foods.

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Conflicts of interest: The authors did not specify any links of interest.

000087 | Efficacy and safety of a home-based immunotherapy program for children

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*Presenting author: D. Denaxa

Background: Although the standard of care for children with peanut allergy is avoidance, clinical trials using commercially prepared oral peanut products have recently started to be translated into hospital physician-supervised peanut oral immunotherapy (OIT). The aim of this retrospective survey was to evaluate the efficacy and safety of peanut food products up-dosing at home as an alternative approach to OIT in maintaining and improving tolerance to peanuts.

Method: A retrospective study of clinical and laboratory data from children with peanut allergy undergoing peanut OIT with home up-dosing using peanut food products as part of routine care at a single tertiary allergy centre between 2016 and 2022. Primary outcome measures were the proportion of children (1) tolerating the equivalent of 300mg of peanut protein, (2) suffering allergic reactions, and (3) withdrawing from the program.

Results: Twenty-two children with peanut allergy (18 with peanut allergy confirmed by physician observed hospital oral challenge, four additional patients with a clear history of allergic reaction to peanut but not challenged in hospital) aged 15 months to 18 years were followed for a median of 16 months. Fifteen (68%) tolerated 300mg or more of peanut protein and 13 (59%) are still engaged in the program. Nine (41%) withdrew, seven because of food aversion. Eight (36%) patients had allergic skin reactions or vomiting self-managed at home. None had respiratory symptoms indicative of anaphylaxis, required administration of intramuscular adrenaline, or needed out-of-hours / emergency care. Most follow-ups were by telephone.

Conclusion: In this cohort of children, home peanut OIT was safe and effective. Larger, multi-centre prospective studies with everyday peanut products are recommended.

Conflicts of interest: The authors did not specify any links of interest.

001405 | Food allergy is associated with increased risk of developing mental disorders: A nationwide study of 603,257 Israelis

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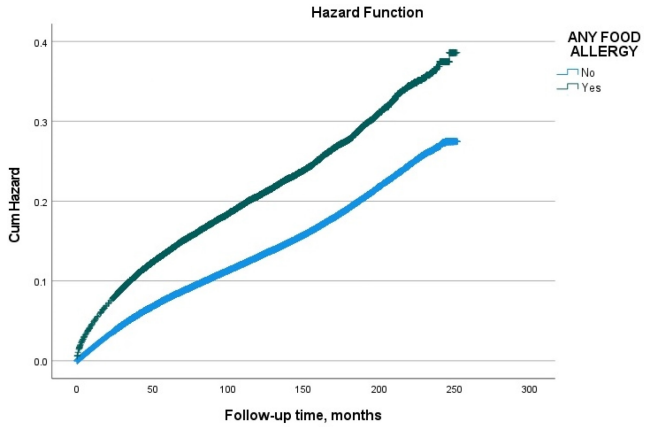
*Presenting author: O. Shamriz

Background: Besides morbidity and mortality due to anaphylactic reactions, food allergies (FA) may also have a direct impact on the patients' social functions, academic achievements, and mental health. Herein, we aimed to analyze the association between FA and mental disorders in a nationwide cohort.

Method: A nationwide study of 603,257 Israelis diagnosed with FA and treated at the "Clalit" Health Medical Organization, Israel, in the period of 2001–2021. Univariable analysis and Cox proportional hazards regression models were used to predict different mental disorders outcomes in patients with FA. Evaluated mental disorders consisted of anxiety, bipolar, psychotic, major depression, eating, post-traumatic stress and sleeping disorders.

Results: The cohort comprised of 603,257 Israelis (53.7% males) diagnosed with FA. Age groups included 0–1 (58.1%), 1–3 (27.1%), 3–18 (12.6%) and >18 years (2.2%). FA were found to be associated with an increased risk of developing anxiety (hazard ratio (HR) = 1.606, $p < 0.001$), major depression (1.071, $p < 0.001$), eating (2.069, $p < 0.001$), post-traumatic stress (1.412, $p < 0.001$) and sleeping disorders (1.468, $p < 0.001$). FA were not associated with increased risk of psychotic and bipolar disorders.

Conclusion: FA are associated with an increased risk of developing mental disorders. This allergy-mental axis should be considered in the management and treatment of patients with FA.



Conflicts of interest: The authors did not specify any links of interest.

001145 | Long-term adherence to oral immunotherapy: A 3-year retrospective, single-center cohort study

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Background: The frequency of adherence to oral immunotherapy (OIT) in relation to the type of allergen, patient characteristics and comorbidities, is still missing. Our aims were to evaluate and compare the adherence and safety of OIT to different food allergens in patients at the maintenance dose phase in a single center.

Method: A total of 256 caregivers of OIT patients from the Bnai Zion Medical Center, received an online questionnaire comprised of 19 items eliciting data about the food allergen, frequency of food allergen consumption, symptoms with food allergen ingestion during the maintenance phase.

Results: The study included data for 213 children, 97 females (45.6%), mean age was 10.04 ±3.5y. Of these, 62 cow's milk (CM) allergy patients (29.2%), 60 peanut allergy patients (28.2%), 54 tree-nut allergy patients (25.3%), 32 sesame allergy patients (15%) and 5 egg allergy patients (2.3%). The median length of follow-up from starting maintenance dose was 19.4 months (range 3- 48 months). Out of 186 patients who ate the allergen maintenance dose (AMD) 82 patients (38.4%) ate only the AMD, 34 patients (15.9%) ate the food allergen without limit, 15 patients (7%) stopped treatment (peanut-6, sesame-5, tree-nut-3, CM-1) and 4 patients ate the AMD irregularly. Reasons for OIT discontinuation were; anaphylaxis (5/15, 33.3%), food allergen aversion (4/15, 26.6%), social difficulty (7/15, 46.7%). Usage of Adrenalin during maintenance phase is a risk factor for stopping OIT ($p = 0.0016$). CM OIT had the higher rate of unlimited allergen eaters; 19 (30.6%) versus 2 sesame patients (6.25%, $p = 0.006$) and 4 peanuts patients (6.6%, $p = 0.0006$). Among patients who consumed the AMD as recommended, 62 out of 202 (30.07%) experienced food allergic reactions. Eight patients (12.9%) required adrenalin (CM- 3, peanuts-3, sesame-1, tree nut-1). More allergic reactions occurred in CM allergic patients compared to sesame and peanut allergic patients (27/61 versus 4 /28 and 14/ 55, $p < 0.01$). Asthma was risk factor for the occurrence of allergic reactions during maintenance phase ($p = 0.02$).

Conclusion: CM OIT patients had the higher rate of OIT adherence despite higher rate of allergic reaction and usage of adrenalin auto-injector.

Conflicts of interest: The authors did not specify any links of interest.

000948 | Persistent milk and egg allergies: Different impact on quality of life in patients and caregivers

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Background: Allergy to milk and egg are most common in childhood, the majority are outgrown but many persist over time affecting their quality of life. We explored the impact in Quality of Life (QoL) in children and caregivers and whether there are differences regarding food and age.

Method: Patients with persistent allergy to milk and egg invited to oral immunotherapy, were submitted before starting the therapy to a complete allergy workup that included a detailed medical

history, severity grading of previous allergic reactions, skin prick test, serum specific IgE to either milk or egg and oral food challenge. Quality of Life was measured using the Food Allergy Quality of Life Questionnaire (FAQLQ) completed by patients and/or parents.

Descriptive statistics included frequency and percent for qualitative variables, and median, first and third quartiles [Q1, Q3] for numerical variables. Qualitative variables were compared with χ^2 or Fisher exact test. Quantitative variables were compared with Mann-Whitney test. Significant level was set at $p < 0.05$. Statistical analysis was done using Python v. 3.8.5.

Results: We included 143 and 147 patients with persistent milk and egg allergy respectively. Baseline population descriptive information can be found in Table 1. Previous allergic reactions were of greater severity with milk (48.1% had severe reactions classified with oFASS-3) in comparison with egg (32.1%) ($p = 0.02$). QoL in all age groups was similar for egg and milk for the total score of FAQLQ and the different domains with the exception of "risk of accidental exposure" which was higher in egg allergic patients 8–12 years-old (4.2 [3.4, 5.3]) than in those allergic to milk of the same age (3.1 [2.1, 5.3]) ($p = 0.04$).

QoL was also found to be worse in patients in the 8–12 years old group with a FAQLQ child form (CF) of 4.16 [2.69, 5.33] combining milk and egg subjects versus 3.19 [2.6, 4.2] in the 13–17 years old group FAQLQ teen form (TF) ($p = 0.05$). FAQLQ parent form had lower scores, 2.75 [2, 4.18], than children and teenagers combined, 3.72 [2.64, 4.98] ($p < 0.01$) (Table 1).

Conclusion: Persistent egg and milk allergy have important negative impact in QoL in both allergic children and parents. The impact in parent´s QoL is lesser that in children and among them the group aged 8–12 is the most negatively affected.

Table 1:

			Milk N= 143	Egg N= 147	p value
Demographics					
Age at baseline (years)			6.7 [5.2-8.9]	8.3 [6.8-10.6]	<0.01
Sex (female)			63 (43.8%)	56 (38.1%)	0.36
Atopic Dermatitis			82 (57%)	113 (79.6%)	<0.01
Asthma before OIT			97 (68.3%)	82 (56.2%)	0.04
Rhinoconjuntivitis before OIT			48 (33.1%)	83 (56.8%)	<0.01
Grading of most severe reaction					
oFASS	Mild	Grade 1	4 (3.1%)	5 (3.6%)	0.02
	Moderate	Grade 2	48 (36.6%)	52 (37.9%)	
		Grade 3	16 (12.2%)	36 (26.3%)	
	Severe	Grade 4	54 (41.2.%)	38 (27.7%)	
		Grade 5	9 (6.9%)	6 (4.4%)	
Diagnostic Tests					
Skin Prick Test milk/eggwhite (mm)			8.5 [6.5, 11.3]	8.75 [7, 10.5]	0.47
IgE milk/eggwhite (kUA/L)			23.1 [6.34, 65.1]	5.1 [2, 14.25]	<0.01
IgE total (kU/L)			273 [111, 637]	411.5 [178.5, 824.8]	<0.01
Quality of Life					
Age groups	**FAQLQ (milk & egg)**		p value	**FAQLQ (milk & egg)**	p value
FAQLQ - CF (8-12y) n=71	4.16 [2.69, 5.33]		0.05	3.72 [2.64, 4.98]	<0.01
FAQLQ -TF (13-17y) n=36	3.19 [2.6, 4.2]				
FAQLQ – Parent form (0-17y) n=108				2.75 [2, 4.18]	

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on drug allergy I

001611 | Rapid drug desensitization in delayed type hypersensitivity reactions to chemotherapeutics

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Background: Desensitization in delayed drug reactions has traditionally used slow protocols extending up to several weeks; RDD protocols have been scarcely reported.

Aim: We aim to present our successful RDD and outcomes in patients who developed delayed type maculopapular eruptions (MPE) due to chemotherapeutics.

Method: This is a single institution-based retrospective study. The medical record of 160 subjects with 1413 RDD cycles with chemotherapeutics between 2011 and 2022 was retrieved from Ege University Dataset. Among them, 8 patients who underwent desensitization due to delayed-type hypersensitivity reactions (> 6 hours) were included in the study.

Results: All skin lesions they had were maculopapular eruptions (MPE). A total of 53 RDD in total was performed with oxaliplatin (26), carboplatin (13), paclitaxel (9), docetaxel (2), liposomal doxorubicin (1), cisplatin (1), gemcitabine (1). A standard 12-step protocol described by Brigham and Women's Hospital group was used with the intravenous drugs. Three (%37.5) cases experienced a total of 8 breakthrough reactions and all of them were immediate or delayed type mild hyperemia in various parts of the body and itching during RDD. All of our patients (%100) completed all RDDs safely and successfully.

Conclusion: There are very few cases of delayed-type reactions to RDD with chemotherapeutics in the literature. This study presents the successful and safe 53 RDDs on delayed type MPE in eight patients. Although slower protocols tend to be more effective than rush protocols for delayed type reactions, for cancer patients RDD can be used as successfully as it is used for immediate hypersensitivity drug reactions.

Table 1. Clinical characteristics of patients and outcomes of RDDs.

	P1	P2	P3	P4	P5	P6	P7	P8
Age	62	52	76	39	45	51	75	69
Sex	Female	Female	Female	Female	Female	Female	Male	Male
Cancer	Lung cancer	Lung cancer	Ovarian cancer	Ovarian cancer	Breast cancer	Liver mass	Lung cancer	Lung cancer
Stage	4	4	4	1	2	2	4	4
RDD Agent	Gemcitabine, Cisplatin	Paclitaxel, Carboplatin	Liposomal doxorubicin	Carboplatin, Paclitaxel	Paclitaxel	Oxaliplatin	Carboplatin	Docetaxel
ST	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Late intradermal positive
DHR at cycle	2	1	2	1	5	1	2	1
DHR type	MPE	MPE	MPE	MPE	MPE, dyspnea	MPE, dyspnea	MPE	MPE
DHR grade*	moderate	moderate	moderate	moderate	moderate	moderate	moderate	moderate
Total RDD number	2	8	1	8	1	26	5	2
RDD protocol	12-step	12-step	12-step	12-step	12-step	12-step	12-step	12-step
Premedication protocol**	Routine	Routine	Routine	Routine	Routine	Routine	Routine	Routine
BT reaction type	hyperemia and itching	hyperemia and itching	hyperemia and itching	hyperemia and itching	hyperemia and itching	hyperemia and itching	hyperemia and itching	hyperemia and itching
BT reaction number	0	0	0	8	0	8	1	0
Outcome of RDD	Completed	Completed	Completed	Completed	Completed	Completed	Completed	Completed

RDD, rapid drug desensitization; ST, skin test; DHR, drug hypersensitivity reactions, BT, breakthrough reactions, MPE, maculopapular eruptions.
*Delayed type drug hypersensitivity reactions; mild, no need to treat; moderate, requirement of treatment; severe, requirement of hospitalization.
**Routine premedication protocol: montelukast, cetirizine, dexamethasone, acetylsalicylic, acid and famotidine for 3 days.

Conflicts of interest: The authors did not specify any links of interest.

000175 | Resolution of NSAID hypersensitivity is associated with chronic spontaneous urticaria remission

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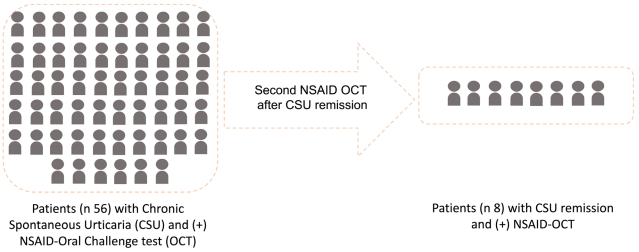
*Presenting author: J. Sanchez

Background: Nonsteroidal anti-inflammatory drugs (NSAID) are one of the most common triggers for exacerbation in chronic spontaneous urticaria (CSU) inducing hives and angioedema. Currently, it is unknown whether hypersensitivity to NSAIDs persists or disappears once the CSU patient goes into remission. The aim of this study was to determine whether remission of CSU is associated with remission of NSAID hypersensitivity.

Method: CSU patients with a positive NSAID challenge test were included and followed up. Once the patient was into CSU remission (at least 6 months without medication, hives, angioedema, or pruritus), a second NSAID challenge test was performed to evaluate the persistence of hypersensitivity. The same NSAID was used in both challenge test and observation period was 6 hours.

Results: Fifty-six CSU patients were included. After CSU remission, forty-eight (86%) patients did not react during second NSAID challenge. Among the patients who tolerated the second challenge, 41 (73.2%) had not previous history of NSAID hypersensitivity before debuting with CSU. Among the 8 patients who did not tolerate challenge, 6 (75%) had hypersensitivity to NSAIDs before starting CSU.

Conclusion: Most of the patients with CSU remission also had remission of NSAID hypersensitivity. The onset period of NSAID hypersensitivity seems to be an important factor related to its remission. The mechanisms of hypersensitivity to NSAIDs during CSU vs hypersensitivity to drugs not associated with CSU may be different.



Conflicts of interest: The authors did not specify any links of interest.

001158 | Experiences with vaccination against COVID-19, the Allergologist's perspective and establishment of a Swedish algorithm

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*Presenting author: A. Csuth

Background: During the first year of mass-vaccination, suspected allergic reactions were reported more often after vaccination against COVID-19 compared to other vaccines. According to our experiences and review of the current literature, we established an algorithm with the Swedish Association for Allergology to evaluate adverse reactions after vaccination.

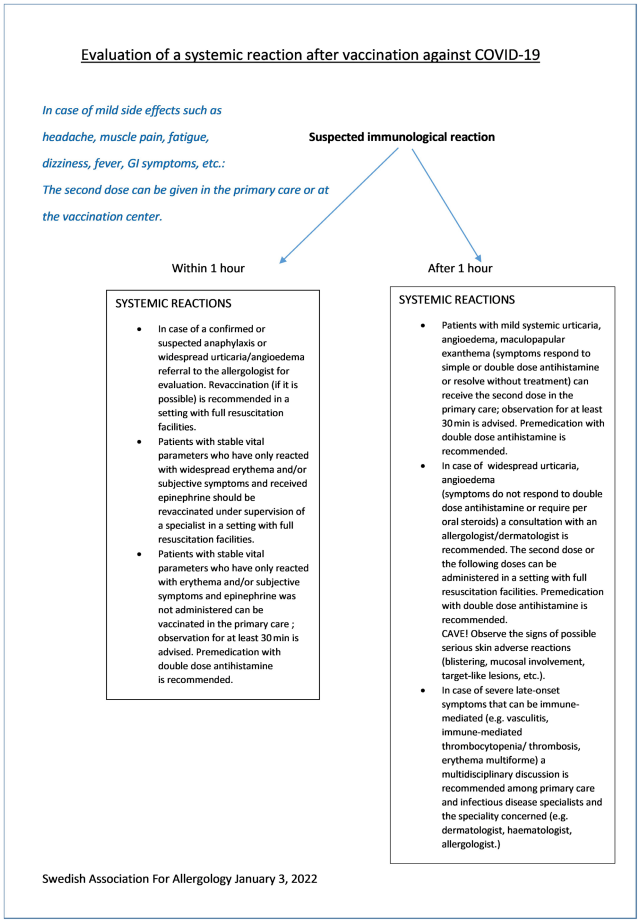
Method: Patients with suspected severe immediate reactions to parenteral drugs were referred to and vaccinated by allergologist without previous skin testing. Persons with suspected hypersensitivity to the vaccine excipients or immediate allergic reactions (*e.g.* anaphylaxis, acute urticaria/angioedema, generalized erythema) to COVID-19 vaccines were evaluated with skin prick tests to the vaccine excipients and the culprit vaccine by an allergologist. In some cases laboratory tests to vaccine excipients (IgE to polyethylene glycol MW 2,000 and 10,000 and basophil activation test) were carried out. Vaccination was offered if the evaluation did not indicate allergy to the vaccine, its excipients and the benefit outweighed the risk. Patients with late-onset urticaria with or without angioedema were evaluated by an allergologist or dermatologist. If severe skin symptoms and organ injury were ruled out the second dose of the vaccine was offered with premedication (antihistamine and/or per oral steroid). Patients with severe late-onset reactions were discussed by multidisciplinary teams, and risk *vs.* benefit evaluations and recommendations regarding future vaccinations were made.

Results: Until now more than 40 patients with immediate reactions, including suspected anaphylaxis to COVID-19 vaccines, and 150 patients with suspected anaphylaxis to parenteral drugs were revaccinated without severe symptoms. No serious adverse events were observed in any patients with late onset urticaria and angioedema.

Patients with more serious systemic reactions were rare and they were evaluated individually.

Conclusion: Immediate allergic reactions and anaphylaxis to COVID-19 vaccines are rare. Different immunological and non-immunological mechanisms (*e.g.* anxiety related reactions) exist that lead to a broad spectrum of adverse events. Excipients were not seen as culprits in our and other cohorts and their role is still uncertain. Establishment of an algorithm based on current research experiences facilitated the evaluation of adverse reactions after vaccination and the revaccination against COVID-19.

Conflicts of interest: The authors did not specify any links of interest.



001648 | Overview and unsuccessful outcomes of chemotherapy rapid drug desensitization

O. Goksel[1,2]; M. Demir[1]; HS. Akten[1]; S. Inan[1]; K. Okan[1]; G. Bogatekin[1]; O. Yildirim[1]; S. Ozgur[2]; R. Gumusburun[1]; T. Goksel[1,2]
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*Presenting author: O. Goksel

Background: Rapid Drug Desensitization (RDD) alters the immune response to the drug and results in temporary tolerance, allowing the patient with a severe drug hypersensitivity reaction to receiving an uninterrupted course of the medication safely. This procedure makes a significant contribution to cancer patients' survival rates in particular.

Method: This is a single institution-based retrospective study. The medical record of 160 subjects with 1413 RDD cycles with chemotherapeutics between 2011 and 2022 was retrieved from Ege University Dataset.

Results: Eight patients had delayed reactions while 152 patients had immediate reactions up to six hours after exposure to the culprit drug. Skin tests were positive with the culprit agent in 41.5%, baseline tryptase level was 8.15 ng/mL (min 1.6, max 132) of 46 cases. A standard 12-step protocol described by Brigham and Women's Hospital group was used with the intravenous drugs. According to Ring and Messer anaphylaxis classification most common breakthrough reactions were Class-1 to Class-3 during RDD. A total of 316 mild to moderate reactions were managed successfully. RDD failed in 3 patients. Two had Grade 4 reactions requiring adrenaline infusion in 2nd and 3rd RDD procedures. One patient could not be overcome with persistent skin and respiratory complications despite a modified, longer 16-step protocol and chose to quit. Three patients were observed to share certain clinical/immunological and disease-related features such as Stage 4 metastatic recurrent cancer and low Karnofsky Performance Scale.

Conclusion: When drug desensitization is performed by experienced centers, the success rate is very high. However, as the number of treatments increased, a failure rate of 1.9% was observed in this series of 1360 chemotherapy cycles. Early identification and description of the commonly shared characteristics of failure will allow us more safety RDD procedures.

Conflicts of interest: The authors did not specify any links of interest.

000755 | Hypersensitivity reactions to biologic agents in patients with severe asthma

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*Presenting author: I. Farinha

Background: The increasing use of biologic agents is associated with consequently an increase in hypersensitivity reactions (HR). The purpose of study was to report our data on suspicion of HR to biologics used for the treatment of severe asthma.

Method: Retrospective review of patients with symptoms of HRs to biologics. The HR were classified into immediate and non-immediate and its severity was classified according to modified Ring and Messmer grading scale. Results of skin tests (prick and intradermal (IDTs), according to ENDA/EAACI recommended concentrations) performed with the implicated biologics and polysorbate were collected. HRs were classified as confirmed based on suggestive clinical history and positive skin or drug provocation tests and as probable according to the suggestive clinical history.

Results: We included 6 patients (2/3 female gender; median age: 29.5 years). Three patients experienced HRs to omalizumab and

three had HSRs to mepolizumab. HRs occurred during the first infusion in one patient, the second infusion in two patients and the rest of HR occurred after various cycles of treatment. All HR were immediate and regarding severity: one patient had grade I reaction, three patients grade II and two patient grade III reaction. Clinically, the most frequent presentation were urticarial rash and respiratory symptoms. The details of allergy investigation are shown in Table 1. Positive skin tests with mepolizumab allowed confirmation of diagnosis of HR in two patients. Drug provocation test with omalizumab were performed in one patient with history of mild reaction and in one patient with negative skin test, both were positive. The diagnosis was confirmed in four patients and it remained probable in two patients. All patients stopped the culprit biologic agent, five switched to alternative biologic and one were currently controlled without biologic treatment.

Conclusion: The diagnosis was confirmed in majority of patients and physicians decided to discontinue the culprit biologic in all patients with suspicion of HR to that biologic agent. HR may limit the use of biologicals, leading to therapy interruption and impaired quality of life, however in our series it was possible to choose an alternative without intercurrences and without the need for drug desensitization. We emphasize the importance of standardizing diagnosing, confirming and managing of HR to biologicals and potential excipients as polysorbate.

Table 1 - Clinical features and allergy investigation of patients with symptoms of hypersensitivity reactions to biologics

Id	Age	Sex	Culprit biologic	Severity reaction	Skin tests to culprit	Skin tests to polysorbate	Provocation test	Alternative biologic
1	16	M	OMZ	II	Neg	Neg	-	Mepolizumab
2	20	M	MPZ	II	Pos	Neg	-	Reslizumab
3	18	F	OMZ	III	Neg	Neg	Pos	Benralizumab
4	39	F	OMZ	I	-	Neg	Pos	-
5	41	F	MPZ	II	-	Neg	-	Dupilumab
6	50	F	MPZ	III	Pos	Pos	-	Reslizumab

Conflicts of interest: The authors did not specify any links of interest.

100289 | Diagnosis and management of hypersensitivity reactions to Radiocontrast media in a regional UK Allergy Centre

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*Presenting author: L. Mutlu

Background: There are 2 major groups of Radiocontrast media (RCM): iodinated contrast materials (ICMs) and Gadolinium-based RCMs (Gad-RCM). Hypersensitivity reactions (HSRs) to ICMs have been reported in 0.5%–3% of patients. Most RCM-induced reactions are non IgE-mediated, however, with the growing use of modern non-ionic iso-osmolar RCM, the proportion of IgE-mediated allergic reactions has increased. A recent EAACI position paper detailed the recommendations on ICM hypersensitivity management (Torres et al, 2022). Previous guidelines as well as recent large case-series support the usefulness of comprehensive allergy assessment by clinical review, skin prick tests (SPT), followed by intradermal tests (IDT) (Rosado Ingelmo et al, 2016; Nucera et al, 2022). The unanimous recommendation is avoidance of the culprit identified positive at skin testing and use of alternative agents. Negative predictive value (NPV) is now quoted > 90% (Srisuwatchari et al, 2022; Shrijivers et al, 2018). Gad-RCM allergy is considered rarer and is usually immediate (Grueber at al, 2021).

Method: Aim was to perform a retrospective critical analysis of all suspected RCM allergy cases referred to our regional specialist Allergy centre between 2010 and 2023, and correlate this to the outcomes of a systematic and standardized allergy work-up. Retrospective data extraction from clinical and electronic patient records was performed. This was registered as an anonymous local audit and ethical approval was not required.

Results: We received a total of 59 referrals.

42 cases were investigated systematically with skin prick testing, followed by intradermal skin tests; of those 36 cases were referred for suspected ICM allergy and 6 cases for Gad-RCM allergy.

7/36 (19.4%) of the ICM cases and 3/6 (50%) of Gadolinium-based RCM cases had positive skin tests. Majority of clinical presentation for ICM allergy were benign cutaneous reactions. All 3 cases of confirmed Gad-RCM allergy had clinical history of immediate systemic reactions; 2 had anaphylaxis with elevated acute tryptase. Outcome and recommendations given were in line with the 2022 EAACI position paper: avoidance of culprit RCM and using skin-test-negative alternative with caution is advised.

Conclusion: RCM allergy is becoming more commonly recognised. Clinical presentation for RCM allergy had a very good correlation with skin tests suggestive of Type-1 HSR aetiology. Further long term follow-up studies are required to reliably ascertain the sensitivity, specificity and negative and positive predictive values of RCM skin tests.

Conflicts of interest: MTK received grants from NIHR, MRC CiC, FSA and GCRF, unrelated to this work. The Allergy and Immunology department where report originates received educational grants from ALK, Allergy Therapeutics, MEDA and other pharmaceutical companies for annual PracticAllergy course. LM, the presenting author has accepted the EAACI conference attendance fees from the company BioCryst.

Flash talks on COVID 19

001674 | SARS-CoV-2 pre-exposure prophylaxis with AZD7442 monoclonal antibodies in inborn errors of immunity with antibody defects

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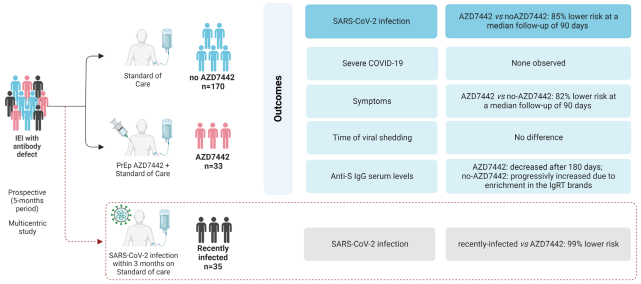
*Presenting author: F. Pulvirenti

Background: The preventive strategy against severe COVID-19 in Inborn Errors of Immunity (IEI) with antibody defects included bivalent vaccines, pre-exposure prophylaxis/treatment with SARS-CoV-2 monoclonal antibodies (mAbs), and early antiviral therapies. In this prospective study, we aimed To assess the effectiveness of the mAbs tixagevimab/cilgavimab (AZD7442) in protecting IEI on immunoglobulins replacement during the Omicron wave.
Method: Prospective study on IEI adults on immunoglobulin replacement. Patients received AZD7442 if not infected by SARS-CoV-2 in the three months preceding. Rates of ARS-CoV-2 infection, COVID-19 severity, and specific anti-Spike IgG were compared between AZD7442 and no-AZD7442 groups and with recently-infected patients.
Results: Six out of thirty-three (18.2%) administered AZD7442 became infected with SARSCoV-2 compared to 54/170 (31.8%) not administered AZD7442. The AZD7442 group was 85% less likely to be infected and 82% less likely to have a symptomatic disease than the no-AZD7442 group within 90 days. None who had received prophylaxis became infected within 75 days, while patients who had not received prophylaxis became infected with a constant trend over time. No mortality/hospitalization was observed. Thirty-five patients were included in the recently-infected group, which was 88% and 92% less likely to have a SARS-CoV-2 infection than the AZD7442 group and the no-AZD7442 group. Among AZD744 recipients, anti-Spike IgG serum reached the highest peak after 7 days, remained high until 150 days, and then decreased to 180 days thereafter. In the no-AZD7442 group, IgG anti-SARS-CoV-2 passively administered by polyvalent immunoglobulins increased over time.
Conclusion: AZD7442 have a protective effect during Omicron emergence in patients with IEI andantibody defects.



Conflicts of interest: The authors did not specify any links of interest.

000151 | Impact of COVID-19 pandemic on childhood asthma and wheezing disorders

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*Presenting author: Y. Xing

Background: Control measures imposed during the COVID-19 pandemic have reduced the transmission of not only SARS-CoV-2 but also common respiratory pathogens. To understand the possible influence of COVID-19 restrictions on future outbreaks of other respiratory infections, it is crucial to examine viral etiologies in susceptible populations, especially children with asthma and related wheezing disorders.
Method: This study prospectively recruited children under 18 years of age who were admitted to Prince and Wales Hospital, the designated hospital for inpatient pediatric services in Hong Kong, between September 2016 to September 2022. Discharge diagnoses included asthma exacerbations, wheezing illness, and bronchiolitis. Nasopharyngeal aspirate specimens were obtained from patients within 12 hours after admission and were then subjected to immunofluorescence-based rapid antigen detection assay followed by respiratory multiplex polymerase chain reaction testing to detect 11 common respiratory viruses including rhinovirus (RV), respiratory syncytial virus (RSV), adenovirus, influenza virus A, B, and C; human metapneumovirus, parainfluenza virus types 1, 2, and 3, and human metapneumovirus. Starting from January 2020, SARS-CoV-2 was detected by RT-PCR tests targeting different regions of the RdRp gene.
Results: We recruited 1355 children (male 67.8%) with 1792 admissions due to wheezing disorders during the study period. The mean age (± standard deviation) at first admission was 3.5 ± 3.2 years. Compared with the pre-pandemic period (September 2016 to January 2020, 40 months), there was a remarkable reduction in wheezing admissions during the COVID-19 pandemic (February 2020 to September 2022, 31 months). In particular, admissions due to "bronchiolitis" dropped from 16 cases per month pre-pandemic to 1.4 cases per month during the pandemic, with the proportion of RSV-induced cases declining from 27.8% to 11.4% ($p = 0.001$). In contrast, RV prevailed with a prevalence rate of 65.5% among children hospitalized for asthma and related wheezing disorders, compared

with 45.4% before the pandemic ($p < 0.001$). After the outbreak of COVID-19, RV has caused more severe cases resulting in PICU admission than in the pre-pandemic period (52.4% *vs*. 19.7%, $p < 0.001$). An unprecedented surge of wheezing admissions, mostly caused by RV, occurred following the relaxation of local COVID-19 restrictions at the end of 2021.

Conclusion: RV was transmitted more efficiently during the COVID-19 pandemic, causing more severe cases in children hospitalized with wheezing disorders than other respiratory viruses. Our results indicate a rebound risk of RV infections following the easing of control measures, highlighting the need for continued surveillance of common respiratory viruses, particularly RV, once COVID-19 restrictions are no longer necessary.

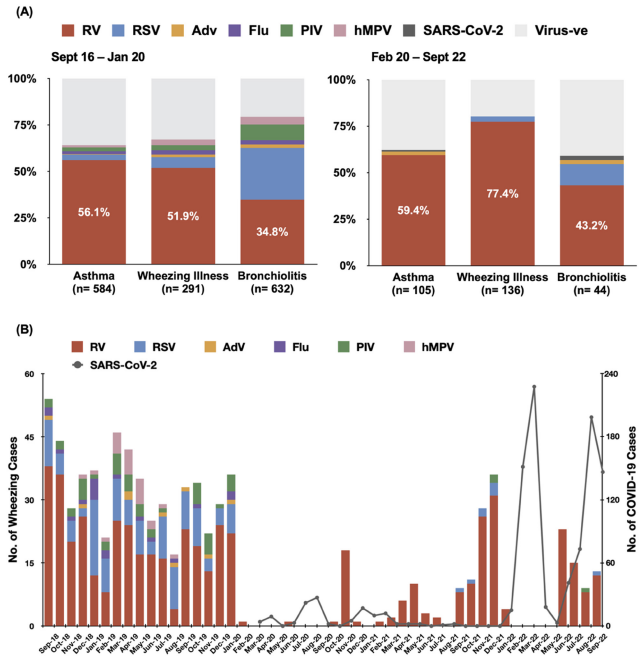

FIGURE 1 Viral etiologies of pediatric patients hospitalized for breathing difficulties. **A:** The prevalence of common respiratory viruses in pediatric patients with asthma and related wheezing disorders pre-pandemic (from September 2016 to January 2020, a total of 40 months) *versus* pandemic period (from February 2020 to September 2022, a total of 31 months). **B:** Monthly distribution of common respiratory virus and SARS-CoV-2 in patients diagnosed with "Wheezing Illness" from September 2018 to September 2022. The first COVID-19 paediatric case was admitted in March 2020. RV, Rhinovirus; RSV, Respiratory Syncytial Virus; AdV, Adenovirus; Flu, Influenza Virus A, B and C; PIV, Parainfluenza Virus types 1-3; hMPV, Human Metapneumovirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease of 2019.

Conflicts of interest: The authors did not specify any links of interest.

001397 | COVID-19 clinical features and prognosis in italian patients with TH2 inflammation treated with biological drugs

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*Presenting author: G. Sambugaro

Background: The clinical management of chronic illnesses, particularly respiratory and allergy disorders, has been significantly impacted by the COVID-19 pandemic. The potential impact of biologics on the clinical course of COVID-19 was once one of the primary worries. Given that Th2 inflammation may play a role in response to viral infections and their course, the impact of biologicals modulating this axis is potentially important in this context. In this multicenter investigation we examined the clinical course of COVID-19 in atopic patients receiving biological therapy and atopic patients not receiving biological therapy.

Method: A questionnaire was given to each patient, asking about the clinical characteristics of the infection (duration of positivity, length of symptoms, severity of symptoms and potential hospitalization, exacerbation of underlying pathology), the therapy being used at the time of infection and any changes to it, and the patient's vaccination status at the time of infection.

Results: The 126 patients we enrolled (89 women) had a prevalence of asthma of 89.7%, nasal polyposis of 31%, chronic spontaneous urticaria of 10.3%, and atopic dermatitis of 5.6%. 59 participants were receiving biological therapy (anti-IgE 27.1%, anti-IL5 27.1%, anti-IL5R 20.3% and anti-IL4/IL13R 25.4%) at the time of infection. In terms of age, sex, BMI, smoking, non-biologic therapies, and OCS use, the two baseline groups were comparable. There were no significant differences between atopic patients receiving any biological therapy and atopic patients not on biologicals for the type, severity and length of symptoms or the duration of swab positivity. Patients with asthma receiving biologic therapy experienced more frequently the worsening of respiratory symptoms than those not on biologicals, although this difference was not significant. There were no significant variations in exacerbation rates comparing the different biologic drug classes. No significant differences emerged in terms of duration of positivity, type and duration of symptoms between subjects on biological and non-biological therapy who had received at least one dose of vaccine. Among unvaccinated patients, on the other hand, there was an increased number of pneumonias and hospitalizations in both groups.

Conclusion: Our study shows that there are no significant differences in the duration of positivity, the duration and severity of symptoms or exacerbations between the biologically treated atopic participants and the control group. In this cohort, anti-Th2 biologic therapy during COVID-19 was generally safe. Their use does not aggravate COVID-19's clinical course or outcomes. Controlled studies, registries or larger real-file studies are needed to draw firm

conclusions about the safety and benefits that these biologic agents may provide during COVID-19 in specific clinical settings.
Conflicts of interest: The authors did not specify any links of interest.

000642 | Access to allergist knowledge important in improving COVID-19 vaccine hesitancy and confidence amongst people managing allergy

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*Presenting author: J. Protudjer

Background: Despite the importance of vaccines to the COVID-19 pandemic response, vaccine hesitancy persists, especially amongst people managing allergic conditions. We aimed to describe the perceptions of COVID-19 vaccines hesitancy and risk amongst adults with, and parents of children with allergic conditions.
Method: We conducted semi-structured qualitative interviews with adults with allergic conditions, and parents of children with allergic conditions, and considered differences between the two groups. We purposively recruited Canadian-based participants via social media and physical posters. All participants (including children in the latter category) had been vaccinated against COVID-19. Transcripts were analysed thematically by two researchers.
Results: Participants included 3 adults, and 5 parents. Themes common to both groups included: Seeking vaccine information from sources perceived to be reputable, including government websites, allergy-specific organizations, scientific resources, medical professionals or their social media and family/friends who work in the scientific/medical field; the counterpoise theme of: Intense emotions as result of ill-advised guidance from reputable sources; and, finally, The benefits of vaccination outweigh the risks.
Themes unique to adults, of whom two did not have an allergist, included: Delayed vaccination due to fear of an allergic reaction, and; Lack of preparedness at vaccination sites for allergic emergencies.
Themes unique to parents, whose children all had allergists, included: Involvement with an allergy community helped to ease anxieties and increase confidence in vaccination, and; Presence of a physician or allergist who is familiar with the participants allergic disease history eased anxieties and increase confidence in vaccination.
Conclusion: In this qualitative study of Canadian-based participants, vaccine confidence amongst adults with allergic conditions was initially shaken due to gaps in resources, professional medical advice, and representation in the literature, and which was further challenged by limited access to allergists. In contrast, parents of children with allergy reported less hesitancy and greater confidence, in part due to access to allergists, but which may have been further enhanced by a later approval of vaccines for children than adults. Enhanced communication from allergists may help diminish vaccine hesitancy amongst adults, and maintain vaccine confidence amongst parents of children with allergic conditions.
Conflicts of interest: Ayel Batac sits on the Manitoba/Saskatchewan Steering Committee for ImmUnity Canada. Elissa Abrams is an employee of the Public Health Agency of Canada; the views expressed are here own and not those of the Public Health Agency. Philippe Bégin reports personal fees from Novartis, Pfizer, Sanofi, ALK-Abelló, Bausch Health and Aralez Pharmaceuticals, as well as grants from DBV Technologies, Regeneron Pharmaceuticals, Novartis, and Sanofi. Moshe Ben-Shoshan sits on the following advisory boards: Stallergenes Greer, Novartis, Sanofi; reports personal fees from Bausch Health, Stallergenes Greer, Novartis, Sanofi; grants from Stallergene Greer; and participated in Novartis, Aimmune Therapeutics, and Sanofi clinical trials. Erika Ladouceur reports consultancy for Novartis. Jennifer Protudjer is Section Head for Allied Health, and a Member of the Board, for the Canadian Society of Allergy and Clinical Immunology; sits on the steering committee for Canada's National Food Allergy Action Plan, and reports consultancy for Nutricia, Novartis, and ALK-Abelló. The remaining authors have no conflicts of interest to report.

000421 | Anaphylaxis and COVID-19 vaccine hesitancy: Update on COVID-19 vaccine confidence among those living with allergy

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*Presenting author: A. Batac

Background: A previous review by our research group found that fear of COVID-19-vaccine-induced allergic reactions was commonly described in the literature, despite the low incidence of anaphylaxis among individuals with allergic disease. Additional studies have been published since our initial review. This review aims to present an update of the peer-reviewed literature on COVID-19 vaccine hesitancy and incidence of allergic reactions.
Method: An *a priori* protocol for this review was drafted in accordance with Arksey and O'Malley's framework for methodological reviews and the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews. Eligible studies

published since our initial review were identified by searching four scientific databases (CINAHL, PsycINFO, MEDLINE, Embase) from 10 March 2022 to 10 November 2022, using an established search process developed by content and methodological experts. This search process provided monthly updates of the literature, which utilized our original search strategy. All eligible articles were independently assessed by two reviewers.

Results: Of the 1117 unique citations identified by our comprehensive search strategy, 54 (4.8%) were included in this review. Consistent with the extant literature, COVID-19-vaccine-induced allergic reactions remain rare in the general population. 35/54 (64.8%) of the included studies highlighted relatively low incidence of serious vaccine-induced allergic reactions, which include anaphylaxis. The literature also suggests that a prior allergic disease history is a risk factor for COVID-19-vaccine-induced allergic reactions. Additionally, the present review identified research on determinants of COVID-19 vaccine hesitancy, in which fear of allergic reactions was identified as a common cause of vaccine hesitancy.

Conclusion: This review update provides further evidence on the rarity of COVID-19-vaccine-induced anaphylaxis. The literature also highlights the significance of combatting misinformation, which has been a hindrance to vaccine confidence. Future studies focusing on combatting and dispelling misinformation could include targeting specific patient populations to ensure that they are properly informed.

Conflicts of interest: Ayel Batac sits on the Manitoba/Saskatchewan Steering Committee for ImmUnity Canada. Elissa Abrams is an employee of the Public Health Agency of Canada; the views expressed are here own and not those of the Public Health Agency. Philippe Bégin reports personal fees from Novartis, Pfizer, Sanofi, ALK-Abelló, Bausch Health and Aralez Pharmaceuticals, as well as grants from DBV Technologies, Regeneron Pharmaceuticals, Novartis, and Sanofi. Moshe Ben-Shoshan sits on the following advisory boards: Stallergenes Greer, Novartis, Sanofi; reports personal fees from Bausch Health, Stallergenes Greer, Novartis, Sanofi; grants from Stallergene Greer; and participated in Novartis, Aimmune Therapeutics, and Sanofi clinical trials. Erika Ladouceur reports consultancy for Novartis. Jennifer Protudjer is Section Head for Allied Health, and a Member of the Board, for the Canadian Society of Allergy and Clinical Immunology; sits on the steering committee for Canada's National Food Allergy Action Plan, and reports consultancy for Nutricia, Novartis, and ALK-Abelló. The remaining authors have no conflicts of interest to report.

001424 | Association between Epstein-Barr-virus reactivation and development of long-covid fatigue

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*Presenting author: J. Rohrhofer

Background: Long-COVID fatigue, a sequel syndrome after SARS-CoV-2 infection including debilitating fatigue, post-exertional malaise (PEM) and neurocognitive disorders, affects 1%–10% of previously infected patients. The disease symptoms largely overlap with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), which is discussed to be post-virally triggered, especially by Epstein-Barr-Virus (EBV) reactivation. In our study, we evaluated whether Long-COVID fatigue onset could be initiated by viral persistence of SARS-CoV-2 or by EBV-reactivation.

Method: We analyzed plasma, stool and throat washing samples of prospectively recruited Long-COVID fatigue patients (n = 30) and compared them to convalescent SARS-CoV-2 infected patients (n = 20). None of the patients suffered severe acute COVID-19 disease course. At the time point of sampling, most study participants were vaccinated against SARS-CoV-2. Also, in most of the participants, infection occurred prior to vaccination. Samples were screened for SARS-CoV-2 RNA and EBV DNA by RT-qPCR and qPCR respectively. Plasma SARS-CoV-2 IgA and IgG, as well as EBV antibodies were tested by commercial ELISA and microarray assays.

Results: We did not detect SARS-CoV-2 RNA in any of the samples. SARS-CoV-2 antibody titers did not differ significantly between the cohorts. However, EBV DNA was detected in throat washing samples in 50% (15/30) of Long-COVID patients compared to 20% (4/20) of convalescent SARS-CoV-2 infected patients (p = 0.0411). EBV loads were not significantly different between the two cohorts and EBV specific antibody titers did not differ between the groups.

Conclusion: All patients, except one fully convalescent SARS-CoV-2 infected patient, were past acute EBV infections. Reactivation of EBV occurs in a significant proportion of the Long-COVID fatigue patients. A complete lack of SARS-CoV-2 RNA did not indicate SARS-CoV-2 persistence. We suggest the observed EBV reactivation to be a co-factor for Long-COVID fatigue. We highly recommend including clinically relevant ME/CFS-related evidence into Long-COVID fatigue research to counteract a large scale sequel of the COVID-19 pandemic.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on immunodeficiencies and autoimmunity

001056 | Comorbidities in angioedema due to C 1-inhibitor deficiency: An italian survey

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*Presenting author: A. Zanichelli

Background: Angioedema due to C1-inhibitor deficiency, hereditary (HAE) or acquired (AAE), is characterized by unpredictable attacks of swelling. C1-inhibitor (C1-INH) plays a pivotal role in several biological pathways. We aimed to investigate the possible association of comorbidities with C1-INH deficiency and long-term prophylaxis (LTP) with androgens (AA) or tranexamic acid (TXA).
Method: This retrospective cohort study involved adult patients with HAE or AAE referring to Milan and Padua angioedema centers in the period 1979–2021. A qualitative comparison was performed to analyze comorbidities vs. general population. The incidence of comorbidities was evaluated during AA or TXA vs. patients without LTP
Results: A total of 500 patients were studied. A greater prevalence among patients was found for: heart diseases (10% vs. 4.8%), acute myocardial infarction (5.4% vs. 1.4%), HCV infection (9.6% vs. 2.5%), and appendectomy (16% vs. 4.3%). In patients with acquired angioedema, a greater prevalence was found for monoclonal gammopathy (53.8% vs. 3.3%) and lymphoproliferative disorders (38.5% vs. 0.4%). In patients taking AA a greater incidence was found for: hypertension (22% vs. 11.1%; OR 1.89), hypercholesterolemia (18.8% vs. 4.7%; OR 3.97), diabetes mellitus (4.8% vs. 1.4%; OR 3.22), hepatic angioma (4.3% vs. 0.6%; OR 8.35), and focal nodular hyperplasia (2.4% vs. 0.4%; OR 6.9). No association with TXA and comorbidities was found
Conclusion: In this large patient population with a rare disease followed for a 43-year period, we found a greater prevalence of comorbidities hitherto unreported in the literature and an association between comorbidities and LTP with AA.
Conflicts of interest: AZ received speaker/consultancy fees and/or was a member of medical/advisory boards for CSL Behring, Shire/Takeda, and SOBI. MC received travel grants from CSL Behring, Menarini, Novartis, Shire-Takeda and consultancy fees from Biocryst, CSL Behring, Shire-Takeda. His Institution received scientific grants from CSL Behring and Shire-Takeda. RS, AM, and VPJ declare that they have no financial competing interests about the topic of this abstract.

000338 | Immunoglobulin replacement therapy: Unexpected preference for intravenous route in a Portuguese adult cohort

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*Presenting author: J. Vieira

Background: Primary immunodeficiencies (PID) are the main indication for immunoglobulin G (Ig) replacement therapy. This treatment decreases the rate of infections and improves patients' quality of life. The route for Ig replacement therapy should be adapted to individual patient´s profile. We aim to assess the experience, motivations, concerns and side effects of patients with PID under intravenous (IV) or subcutaneous (SC) Ig replacement therapy.
Method: Observational study including 67 patients under IV/SC Ig replacement therapy followed in a tertiary PID centre. Patients filled in an online questionnaire addressing clinical and demographic features (Table 1).
Results: We included 41 patients under IVIg, with mean age at the beginning of treatment: 33 years old. The most frequently reported side effects were fatigue (*n* = 20); headache (*n* = 6); drowsiness (*n* = 6). To prevent these effects, pre-medication was precribed in 16 patients. The most frequent reasons explaining preference for IVIg were: monthly administration (*n* = 28); more frequent contact with medical/nursing team (*n* = 22); fear of self-administration of SCIg (*n* = 11). Most patients (87.8%) consider IVIg administration at the hospital simple and practical and 65.9% do not want to try SC route.
Twenty-six patients were under SCIg, with a mean age at the beginning of treatment: 30 years old. Most frequently reported side effects were: local oedema (*n* = 18); local erythema (*n* = 8); fatigue (*n* = 4). Main reasons/motivations for preference of SCIg were: less time-consumption (*n* = 18); more time flexibility (*n* = 17); fewer trips to the hospital/lower infections risk (*n* = 11). Main concerns regarding SC Ig were the risk of adverse reactions (*n* = 7); administration errors (*n* = 5); difficulties with compliance (*n* = 4). 50% do not report concerns related to SC administration and 65% considered this route simple and practical, and valued the training provided by the nurses and the possibility of practicing self-administration at the hospital.
Conclusion: This is a pioneer study addressing PID patients' preferences regarding Ig replacement therapy administration route, thus providing important and original data for national and international reflection. We highlight the elevated proportion of patients in our centre who prefer IVIg route. Individual analysis of patients' answers will be helpful for optimising personalized treatment and improving quality of life.

Table 1 – Clinical and demographic characterization of the population.

	Intravenous Immunoglobulin G	Subcutaneous Immunoglobulin G
N	41	26
Female, n (%)	27 (65,9%)	11 (42%)
Age, years old (min-max)	46 (24-80)	39 (23-63)
Education Degree	University education – 43,9% High school – 19,5% Elementary school – 36,6%	University education – 61,5% High school – 26,9% Elementary school – 11,6%
Professional Situation	Employed – 58,5% Unemployed – 12,2% Retired – 24,4% Student – 4,9%	Employed – 96,2% Unemployed – 3,8%
Primary Immunodeficiency Diagnosis	Common variable immunodeficiency – 30 X-linked agammaglobulinemia – 4 Specific antibody deficiency – 4 Hyper IgM syndrome – 1 WHIM syndrome – 1 STAT 1 gain-of-function – 1	Common variable immunodeficiency – 17 Specific antibody deficiency – 4 X-linked agammaglobulinemia – 2 Good syndrome - 2 Hyper IgM syndrome – 1

STAT-1 – Signal transducer and activator of transcription-1
WHIM – Warts, hypogammaglobulinemia, infections, myelokathexis

Conflicts of interest: The authors did not specify any links of interest.

001005 | Long-term effectiveness and safety of lanadelumab regardless of baseline attack rate: Pooled analysis of the enable and empower studies

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[1]HRZM Hemophilia Center Rhein Main, Mörfelden-Walldorf, Germany; [2]Takeda Development Center Americas, Inc., Lexington, USA; [3]Takeda Pharmaceuticals International AG, Zürich, Switzerland; [4]University of Lübeck, Lübeck, Germany; [5]Laval University, Centre Hospitalier Universitaire de Québec (CHUQ), Québec, Canada; [6]Massachusetts General Hospital, Harvard Medical School, Boston, USA; [7]Ospedale Luigi Sacco, ASST Fatebenefratelli Sacco, University of Milan, Milan, Italy

*Presenting author: A. Zanichelli

Background: Patients with hereditary angioedema (HAE) may have varying levels of disease activity, which can include attack frequency. To assess if lanadelumab effectiveness and safety are impacted by baseline disease activity, we analysed pooled data from the real-world ENABLE (NCT04130191) and EMPOWER (NCT03845400) studies.

Method: This pooled analysis included patients with HAE Type I/II aged ≥12 years who received lanadelumab according to approved product labelling in the Phase IV ENABLE and EMPOWER studies and had available baseline attack rate. Patients were divided into subgroups by their baseline disease activity (low: <1 attacks/month, moderate: ≥1 to <2 attacks/month, high: ≥2 to <3 attacks/month, very high: ≥3 HAE attacks/month). Lanadelumab effectiveness was evaluated as the incidence rate ratio (IRR) of HAE attack rates on lanadelumab use vs baseline. Data on treatment-emergent adverse events (TEAEs), excluding HAE attacks, were also collected.

Results: A total of 122 patients were included; 21 had low, 19 moderate, 15 high, 67 very high disease activity. At baseline, any medical history events were reported in 16 (76.2%), 17 (89.5%), 12 (80.0%) and 47 (70.1%) patients from low, moderate, high and very high disease activity subgroups, respectively. The mean ± SD duration of follow-up ranged from 369.8 ± 211.2 to 476.7 ± 254.3 days across subgroups. Marked reductions in mean HAE attack rate vs baseline were observed regardless of baseline disease activity (low activity: 58%, moderate activity: 78%, high activity: 74%, very high activity: 92%; **Figure**). TEAEs were primarily non-serious, mild/moderate in severity and not related to lanadelumab in all subgroups (low activity: 18 TEAEs in 8 patients, 100.0% non-serious, 100.0% mild/moderate, 88.9% not related to lanadelumab; moderate activity: 12 TEAEs in 8 patients, 100.0% non-serious, 91.7% mild/moderate, 83.3% not related to lanadelumab; high activity: 19 TEAEs in 7 patients, 94.7% non-serious, 89.5% mild/moderate, 89.5% not related to lanadelumab; very high activity: 110 TEAEs in 35 patients; 97.3% non-serious, 94.5% mild/moderate, 79.1% not related to lanadelumab). No TEAEs resulted in discontinuation.

Conclusion: Lanadelumab reduced HAE attack rates versus baseline across the 4 disease activity subgroups over >1 year of treatment among patients in the real-world clinical practice. Safety of lanadelumab was consistent across all subgroups; most TEAEs were non-serious, mild/moderate in severity and not related to lanadelumab.

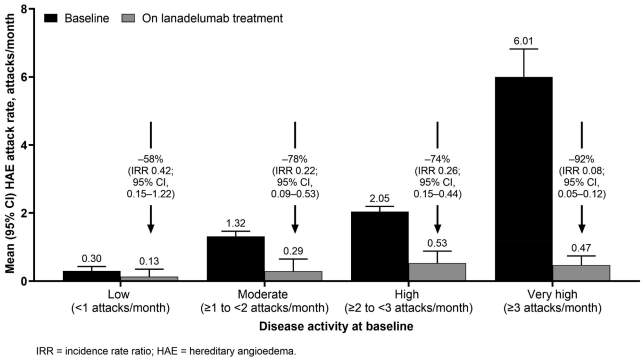

Figure. Attack rate reduction on lanadelumab treatment by baseline disease activity.

Conflicts of interest: I. Martinez Saguer has received honoraria, research funding, consultancy fees and travel grants from and/or has participated in advisory boards for BioCryst, CSL Behring, Pharming and Takeda. T. Andriotti, D. Nova Estepan, A. Yegin and J. Botha are employees of and hold stock/options in Takeda. A. Recke has received research grants from Deutsche Forschungsgemeinschaft and Euroimmun; other research support from Novartis, Pharming, Stallergenes Greer and Takeda; honoraria from BENCARD, BioCryst, Euroimmun, Novartis and Takeda; and served as a consultant or participated in advisory boards for BioCryst, Novartis and Takeda. P.J. Busse has received research support and served on advisory boards for BioCryst, CSL Behring and Takeda; and is a consultant for CVS Pharmacy, Medscape, Novartis and Regeneron. R. Gagnon has received honoraria from Novartis, Pfizer and Takeda, and has participated in trials within the last 2 years for AstraZeneca, BioCryst, CSL Behring, DBV, Green Cross, Merck, Regeneron, Sanofi, Stallergenes and Takeda. A. Banerji has received institutional research/study support from BioCryst and Takeda; and/or honoraria for consulting from BioCryst, CSL Behring, KalVista, Pharming, Pharvaris and Takeda. A. Zanichelli has received speaker/consultancy fees from BioCryst, CSL Behring, Pharming and Takeda.

001114 | An observational retrospective study on vaccinations in immunocompromised patients

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*Presenting author: R. Scarmozzino

Background: We aimed at analyzing adverse events following immunization (AEFI) in patients with primary immunodeficiencies to evaluate the safety of vaccination in this population.
Method: we performed an observational retrospective study collecting clinical data and vaccination records of 83 patients with confirmed primary immunodeficiencies referred to our Outpatient Immunology Unit in the period 2004–2022. The following data were analyzed: age, sex, mandatory and recommended vaccinations according to our regional immunization schedule, AEFI, with onset up to 6 weeks after administration. Vaccination outcome before and after diagnosis of immunodeficiency was evaluated. Adverse reaction severity was classified as common, relevant or serious according to criteria defined by the Green Channel University Hospital Immunization Consultancy Clinic
Results: A total of 83 records were evaluated, including 34 males and 49 females, from the age of 19 up to 84 years old, with diagnosis of primary immunodeficiencies (PID) distributed as follows: 18 Common Variable Immunodeficiency (CVID), 38 isolated IgA deficiency, 15 hypogammaglobulinemia, 4 IgG subclass deficiency, 2 IgA and IgG subclass deficiency, 1 IgA and B-cell and T-cell deficiency, 1 IgA deficiency with low NK and CD4, 1 T cell deficiency, 1 IgM and B cell deficiency, 1 B cell deficiency with normal immunoglobulins, 1 IgA and IgM deficiency. Mean age at diagnosis was 38. Seventy-eight patients documented one or more vaccine administrations after diagnosis of PID, while 5 received all the vaccines before immunodeficiency diagnosis. A total of 603 doses of vaccines were administered after diagnosis and 693 before diagnosis, for a total of 1296 doses. Injection site or common systemic AEFI were documented in 9 medical records, none of which were serious or clinically relevant reactions. Vaccines involved in AEFI were Meningococcal Group B (MenB) in 4 cases, and one reaction for each of the following vaccines: Meningococcal ACWY vaccine (Men-ACWY), Oral Polio Vaccine (OPV), Diphtheria, Tetanus and Pertussis combined vaccine (dTaP), Pneumococcal Conjugate Vaccine (PCV-13), 2009 H1N1 vaccine.
Conclusion: These data show that only a minority of patients with PID manifested common non serious AEFIs, confirming the safety of vaccinations in this population.
Conflicts of interest: The authors did not specify any links of interest.

000902 | Quality of life during lanadelumab treatment in patients with hereditary angioedema: 24-month results from the enable study

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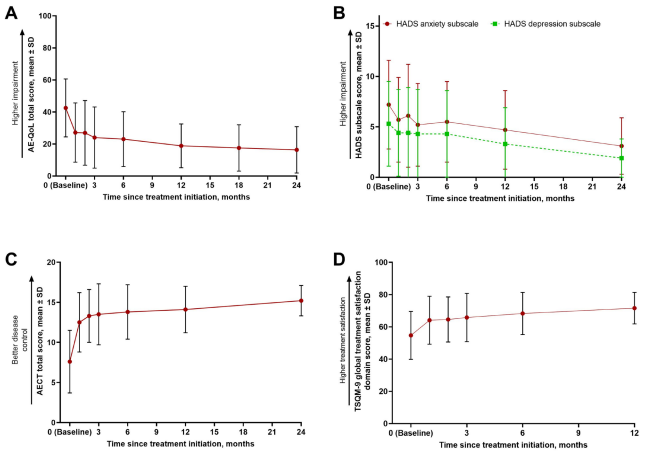
*Presenting author: M. Magerl

Background: Patients with hereditary angioedema (HAE) suffer from recurrent swelling attacks, which are unpredictable, disabling, potentially life-threatening and result in impaired quality of life (QoL). A secondary objective of the Phase IV non-interventional, prospective, multicenter ENABLE Study (NCT04130191) is to evaluate the effect of lanadelumab treatment on QoL in patients with HAE in real-world clinical practice. We report results of patient-reported outcomes (PRO) over 24 months of lanadelumab treatment, expanding upon 12-month data reported previously.
Method: Patients with HAE Type I/II aged ≥12 years who initiated lanadelumab treatment according to approved product labelling are recruited in Austria, Germany, Israel, Kuwait, Italy, Spain and Switzerland. PRO measures include the Angioedema Control Test (AECT), Angioedema Quality of Life (AE-QoL) questionnaire, Hospital Anxiety and Depression Scale (HADS) and Treatment Satisfaction Questionnaire for Medication (TSQM-9). PRO data are collected at enrolment, months 1, 2, 3, 6, and every 6 months thereafter up to month 24 (in patients who entered the study on or after 1 March 2021) or 36 (in patients who entered the study before 1 March 2021).
Results: A total of 109 patients with ≥1 dose of lanadelumab and ≥1 effectiveness assessment were included in this interim analysis (11 December 2019 to 1 April 2022). Over the first 24 months of study, the mean ± SD total AE-QoL score decreased from 42.5 ± 18.1 at baseline to 16.3 ± 14.5 at month 24, indicating improved QoL (**Figure**). The mean ± SD HADS anxiety and depression scores decreased from 7.2 ± 4.4 and 5.3 ± 4.2 at baseline, respectively, to 3.1 ± 2.8 and 1.9 ± 1.9 at month 24, respectively. The mean ± SD AECT score increased from 7.6 ± 3.9 at baseline to 15.2 ± 1.9 at month 24; AECT total score ≥10 indicates well-controlled disease. The increase in the mean ± SD TSQM-9 global satisfaction score from 54.7 ± 14.9 at baseline to 71.6 ± 9.8 at month 12 indicated increased patient satisfaction with treatment.
Conclusion: The data from the real-world ENABLE Study demonstrated improvements in QoL, anxiety, depression and angioedema control over 24 months of treatment with lanadelumab as well as

increased treatment satisfaction over 12 months of treatment with lanadelumab.



AECT = Angioedema Control Test; AE-QoL = Angioedema Quality of Life; HADS = Hospital Anxiety and Depression Scale; TSQM-9 = Treatment Satisfaction Questionnaire for Medication.

Figure. AE-QoL total score (A), HADS anxiety and depression subscale scores (B), AECT total score (C), and TSQM-9 global treatment satisfaction domain score (D) over time in the ENABLE Study.

Conflicts of interest: I. Martinez-Saguer has received honoraria, research funding, consultancy fees and travel grants from and/or has participated in advisory boards for BioCryst, CSL Behring, Pharming and Takeda. M. Magerl has received research grant support and/or speaker/consultancy fees from BioCryst, CSL Behring, Pharming and Takeda. T. Andriotti, J. Botha, M. Watt and A. Yegin and are employees of and hold stock/options in Takeda. N. Agmon-Levin does not have any conflicts to disclose. M. Maurer is or recently was a speaker and/or advisor for BioCryst, CSL Behring, KalVista, Moxie, Pharming, Pharvaris and Takeda, and has received research funding from BioCryst, CSL Behring, Moxie, Pharming and Takeda.

000847 | Real-world effectiveness and safety of lanadelumab for prophylaxis of hereditary angioedema attacks: 2-year interim results from the enable study

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*Presenting author: A. Kessel

Background: The ENABLE Study (NCT04130191) is a Phase IV non-interventional, prospective, multicenter study evaluating the long-term effectiveness of lanadelumab in real-world clinical practice. Results from this interim analysis (IA; 11 December 2019 to 1 April 2022) expand on previously reported 12-month data.

Method: Patients aged ≥12 years with hereditary angioedema (HAE) Type I/II who initiated treatment with lanadelumab according to approved product labelling are recruited from Austria, Germany, Israel, Kuwait, Italy, Spain and Switzerland. The primary effectiveness outcome is the incidence rate ratio (IRR) of HAE attacks on lanadelumab treatment compared with baseline. Safety of lanadelumab is evaluated by summarizing treatment-emergent adverse events (TEAEs).

Results: In this IA, lanadelumab effectiveness was evaluated in 109 patients (mean ± SD age 41.4 ± 14.9 years, mean ± SD time from HAE symptom onset to diagnosis 8.2 ± 10.7 years, 64.2% female, 99.1% White, 76.1% had medical history events at any time prior to enrolment). In the 3 months prior to enrolment, 74.3% of patients used HAE-specific medications other than lanadelumab for on-demand treatment or long-term prophylaxis. The mean ± SD time on lanadelumab treatment was 436.1 ± 233.5 days. HAE attack rate decreased from a mean (95% CI) of 4.06 (3.47–4.74) at baseline to 0.48 (0.37–0.63) attacks/month on lanadelumab treatment (88% reduction, IRR [95% CI]) 0.12 [0.09–0.16]; **Figure**); 91 (86.7%) patients had ≥70% reduction in HAE attack rate versus baseline. A total of 151 TEAEs were reported among 54/117 (46.2%) patients. Most of TEAEs were mild (53.6%) or moderate (40.4%), non-serious (97.4%) and not related to lanadelumab treatment (80.8%). There were no discontinuations from the study or lanadelumab treatment, no deaths due to TEAEs, and no patients reported serious TEAEs related to lanadelumab. The most frequent treatment-related TEAEs belonged to the MedDRA System Organ Class (SOC) General disorders and administration site conditions (19 events in 17 patients); these included injection site erythema, pain and/or reactions, among others; none of these were considered to be severe.

Conclusion: Real-world evidence from a 2-year interim analysis of the ENABLE Study demonstrated marked reduction in HAE attack rate in patients treated with lanadelumab. The most frequent treatment-related TEAEs belonged to the SOC General disorders and administration site conditions, consistent with pivotal lanadelumab studies.

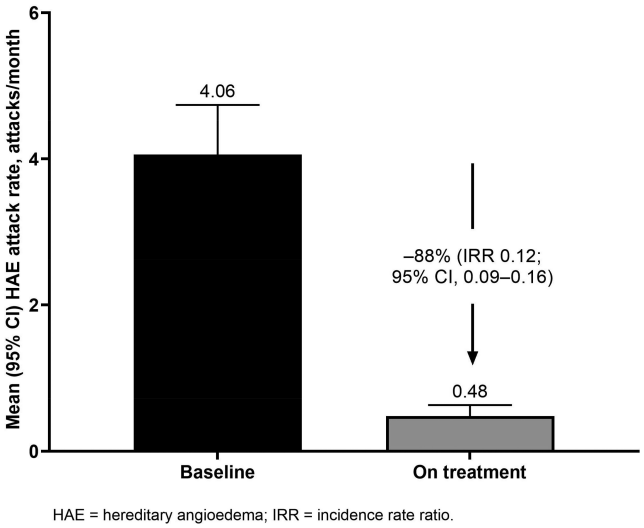

Figure: Attack rate reduction on lanadelumab treatment in the ENABLE Study

Conflicts of interest: W. Wulleimin has received research grant support and speaker/consultancy fees from CSL Behring and Takeda for the research foundation of the Hematology Department at Luzerner Kantonsspital, Lucerne, Switzerland. T. Andriotti, A. Yegin and J. Botha are employees of and hold stock/options in Takeda. A. Kessel has received travel grants from Pharming and Takeda; honoraria from CSL Behring and Takeda. T. Kinacyian has received research funding, speaker honoraria/consultancy fees and travel grants from BioCryst, CSL Behring, KalVista, Pharming and Takeda. M. Cancian reports personal fees from BioCryst, CSL Behring, KalVista and Takeda. I. Martinez-Saguer has received honoraria, research funding, consultancy fees and travel grants from and/or has participated in advisory boards for BioCryst, CSL Behring, Pharming and Takeda.

001199 | **Relationship between autoimmune manifestations and genetic disorders in patients with pid: A single center 10-year experience**

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*Presenting author: M. E. Gerek

Background: In the 2022 classification of the International Union of Immunological Societies, 485 human inborn errors of immunity were described, to which 55 new monogenic defects were added. (1). The newly discovered mutations will accelerate the process of disease diagnosis. In addition, many studies are being conducted to elucidate the relationship between new mutations and autoimmune diseases. We conducted this study to investigate the prevalence of autoimmune diseases and genetic mutations in patients diagnosed with primary immunodeficiency (PID) who were followed up in our clinic.

Method: A total of 74 patients with PID were enrolled in the present study. Twenty-five patients (33.7%) had an autoimmune disease. In these patients, the next-generation sequencing method generated and analyzed a targeted multigene panel associated with primary immunodeficiency.

Results: The median age was 35 years (IQR, 19–76 years), and 35 (47%) were female. A total of 74 PID patients, 15 (20.3%), had autoimmune cytopenia (autoimmune hemolytic anemia, immune thrombocytopenic purpura), 5 (6.8%) had rheumatologic diseases (Sjögren's syndrome, Raynaud's disease, Ankylosing spondylitis), 3 (4.1%) had autoimmune thyroiditis, 2 (2.7%) had Crohn's disease, 2 (2.7%) had granulomatous and lymphocytic interstitial lung diseases, 2 (2.7%) had lymphoma, and 1 (1.4%) had alopecia (Figure 1). Ten (40%) of the individuals with autoimmune diseases had pathogenic mutations, and 7 (28%) had variations of unknown significance (VUS). No mutations were detected in eight patients (32%) (Table 1). Three patients with a pathogenic mutation of the TNFRSF13B gene, all of whom had been diagnosed with immune thrombocytopenic purpura (ITP), tested positive for the mutation. One of the two thyroiditis patients had a mutation in the CD3G gene. Homozygous NLRC4 mutation was detected in one of the 2 Crohn's patients. One patient with LRBA mutation was diagnosed with non-Hodgkin lymphoma.

Conclusion: In our study, 25 individuals were found to have autoimmune diseases. Ten of these patients have pathogenic mutations. TNFRSF13B, CD3G, NLRC4, and LRBA mutations are conditions associated with autoimmune diseases (2, 3, 4, 5). Studies in larger groups of patients and including newly discovered mutations will increase our knowledge of similar associations.

Patient No	Age	Gender	Autoimmune diagnosis	Gene	Patterns of inheritance	Variant coordinates	Zygosity	Genetic variant	Classificatio n
Pt 1	28	M	ITP	TNFRSF13B	AD/AR	c.310T>C	Heterozygous	Missense	Pathogenic
Pt 2	55	M	ITP	TNFRSF13B	AD/AR	c.51G>A	Heterozygous	Missense	Pathogenic
Pt 3	33	F	ITP	TNFRSF13B	AD/AR	c.452C>T	Heterozygous	Missense	Pathogenic
Pt 4	22	F	ITP , AIHA	PRF 1	AR	c.1047G>A	Heterozygous	Missense	Pathogenic
Pt 5	48	M	NHL	LRBA	AR	c.6100G>A	Heterozygous	Missense	Pathogenic
Pt 6	33	F	AIHA, Raynaud's disease	CSCR1 (AD/AR)	AR	c.1444delG	Homozygous		Pathogenic
Pt 7	19	M	Crohn's disease, AIHA, AS	NLRC4	AD			Missense	Pathogenic
Pt 8	43	F	Sjögren's syndrome	USB1	AR	c.413C>T	Heterozygous	Missense	Pathogenic
Pt 9	36	M	NHL, GLILD	IFNGR1	AR	c.85+302T>A	Heterozygous	Intronic	Pathogenic
Pt 10	27	F	Thyroiditis	CD3G	AR	c. 80-1G>C	Homozygous	Splice Acceptor	Pathogenic
				NCF4	AR	c.617A>G	Heterozygous	Missense	VUS
				NCF4	AR	c.884C>T	Heterozygous	Missense	VUS
Pt 11	25	F	AIHA	RPL5	AD	c.233C>T	Heterozygous	Missense	VUS
Pt 12	31	F	AIHA, ITP, GLILD	RAG1	AR	c.1702G>A	Heterozygous	Missense	VUS
Pt 13	25	M	ITP, AIHA	LRBA	AR	c.4522C>G	Heterozygous	Missense	VUS
Pt 14	23	M	AIHA	DOCK8	AR	c.3212T>C	Heterozygous	Missense	VUS
				FOXP3	XLR	c.711+6C>T	Heterozygous	Intron, Splice Region	VUS
Pt 15	60	F	MS	TNFRSF13B	AD/AR	c.452C>T	Heterozygous	Missense	VUS
				DOCK8	AR	c.3277G>A	Heterozygous	Missense	VUS
Pt 16	24	M	AIHA	DOCK8	AR	c.1972A>G	Homozygous	Missense	VUS
				IL10RA	AR	c.781C>T	Heterozygous	Missense	VUS
Pt 17	35	F	Thyroiditis	IFNGR2	AR	c.722A>T	Heterozygous	Missense	VUS
				DOCK8	AR	c.5378T>C	Heterozygous	Synonym	VUS
Pt 18	23	M	Ankylosing spondylitis	NO MUTATION DETECTED					
Pt 19	24	M	Autoimmune hepatitis						
Pt 20	56	F	Sjögren's syndrome						
Pt 21	38	F	ITP						
Pt 22	46	M	Alopecia						
Pt 23	55	F	Sjögren's syndrome						
Pt 24	38	F	Thyroiditis						
Pt 25	34	M	Crohn's disease, ITP						

Table-1

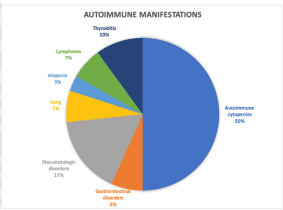

Figure-1

Conflicts of interest: The authors did not specify any links of interest.

000329 | Results from a randomized, double-blind, placebo-controlled, phase 1 trial evaluating sebetralstat pharmacokinetics, pharmacodynamics, and safety/tolerability in healthy Japanese, Chinese, and white adults

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*Presenting author: M. Hide

Background: Hereditary angioedema (HAE) is a genetic disorder manifesting as unpredictable attacks of tissue swelling caused by uncontrolled activation of the kallikrein kinin system. KONFIDENT is a phase 3 trial evaluating the novel plasma kallikrein (PKa) inhibitor sebetralstat as an oral on-demand treatment for HAE attacks. To support global expansion, a phase 1 ethnobridging trial was performed to evaluate pharmacokinetics (PK), pharmacodynamics (PD), and safety/tolerability of sebetralstat in Japanese and Chinese adults compared with those observed in White adults.

Method: Healthy adults (aged 18–55) who self-reported as Japanese, Chinese, or White were eligible to participate in a single-center, randomized, double-blind, placebo-controlled, phase 1 trial. Japanese and Chinese participants must have had both grandparents born in their respective countries and participants must not have lived outside that country for ≥10 years. Participants were randomly assigned to receive a single oral dose of sebetralstat (300 mg, 600 mg, or 1200 mg) or placebo while fasting. PK was assessed using maximum plasma concentration (C_{max}), time to C_{max} (T_{max}), and area under the concentration-time curve (AUC). PD was assessed using dextran sulfate (DXS)–stimulated plasma kallikrein activity levels in plasma.

Results: Japanese, Chinese, and White (n = 24 each) participants completed the study. Baseline characteristics were generally similar across populations. After oral administration of 600 mg of sebetralstat, the geometric mean C_{max} (6178 ng/mL [CV%: 51.8] for Japanese, 5197 ng/mL [92.0] for Chinese, and 5961 ng/mL [41.4] for White) and $AUC_{0\text{-inf}}$ (16,600 h*ng/mL [64.8], 16,120 h*ng/mL [42.9], 16,400 h*ng/mL [31.8]) were comparable among the cohorts (Table 1). Sebetralstat 600 mg resulted in ≥95% geometric mean inhibition of stimulated PKa activity by 30 minutes. This near-complete inhibition was maintained through to the 4-hour time point in all 3 cohorts. Single doses of sebetralstat 300 mg or 1200 mg also showed consistent PK and PD profiles between each studied population. Sebetralstat was generally safe and well tolerated in the studied populations.

Conclusion: Sebetralstat was similarly well tolerated in healthy Japanese, Chinese, and White adults, and PK and PD were comparable across populations. These findings support continued global expansion of the KONFIDENT phase 3 trial assessing the safety and efficacy of sebetralstat for the treatment of on-demand attacks in HAE.

Table 1. **Pharmacokinetic Parameters in Healthy Adults Treated with Sebetralstat**

	Japanese	Chinese	White
Sebetralstat 300 mg	n=6	n=6	n=6
C_{max}, ng/mL, geometric mean (%CV)	2832 (90.4)	3173 (20.6)	2243 (53.7)
T_{max}, h, median	1.26	1.00	1.29
$AUC_{0\text{-inf}}$, h*ng/mL, geometric mean (%CV)	7495 (50.4)	7725 (22.7)	8190 (22.2)
Sebetralstat 600 mg	n=6	n=6	n=6
C_{max}, ng/mL, geometric mean (%CV)	6178 (51.8)	5197 (92.0)	5961 (41.4)
T_{max}, h, median	0.99	0.64	1.00
$AUC_{0\text{-inf}}$, h*ng/mL, geometric mean (%CV)	16,600 (64.8)	16,120 (42.9)[a]	16,400 (31.8)[a]
Sebetralstat 1200 mg	n=6	n=6	n=6
C_{max}, ng/mL, geometric mean (%CV)	7736 (111.8)	7645 (78.8)	5746 (31.6)
T_{max}, h, median	0.75	1.16	1.02
$AUC_{0\text{-inf}}$, h*ng/mL, geometric mean (%CV)	21,800 (39.0)[b]	30,530 (49.2)	24,450 (35.5)

[a]n=5 for $AUC_{0\text{-inf}}$; [b]n=4 for $AUC_{0\text{-inf}}$.

Conflicts of interest: MH has received consulting fees from KalVista Pharmaceuticals, BioCryst, Takeda, and Torii; has received payments or honoraria for lectures, presentations, or manuscripts from KalVista Pharmaceuticals, BioCryst, CSL-Behring, Takeda, and Torii; has received support for meeting attendance from KalVista Pharmaceuticals and Takeda; has received equipment, materials, drugs, or other services from Takeda (Shire); and served a leadership or fiduciary role in the World Allergy Organization and the European Academy of Allergy an Clinical Immunology. MI, EH, and SLH are employees and shareholders of KalVista Pharmaceuticals. SJ and EY received funding from KalVista Pharmaceuticals for this project, paid to their institution. EJD was an employee of KalVista at the time of study execution and holds KalVista shares. DH has received consulting fees from Takeda and Torii; has received payments or honoraria for lectures, presentations, or manuscripts from KalVista Pharmaceuticals, BioCryst, CSL Behring, Takeda, and Torii; support for meeting attendance from Takeda; and serves a leadership or fiduciary role in the Japanese Association for Complement Research.

001676 | Chronic lung disease, age, and IgA influence perturbation of respiratory microbial ecosystems in common variable immunodeficiency

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*Presenting author: F. Pulvirenti

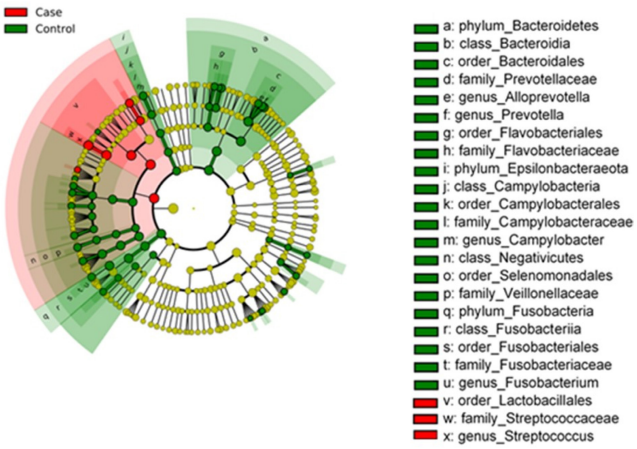
Background: The respiratory tract microbiota is essential for human health and well-being and is driven by genetic, lifestyle and environmental factors. Patients with Common Variable Immunodeficiency (CVID) suffer from recurrent respiratory and intestinal tract infections, leading to chronic lung diseases and increasing mortality. Alterations in gut microbiota have been extensively analyzed while data on respiratory microbiota are scarce. Here we aimed to

characterize the bacterial communities in the oropharyngeal respiratory tract obtained from adults with CVID.

Method: The microbiota of 72 oropharyngeal samples from adult patients and 26 age-matched healthy volunteers were collected in a 12-month prospective study. Samples were analyzed by sequencing of the bacterial 16S ribosomal RNA gene and then processed using Quantitative Insights Into Microbial Ecology pipeline. Metagenomic analysis data were confirmed by a machine learned-based comparative metagenomics tool. A dysbiosis-index was calculated from the taxonomic profile.

Results: Compared to controls, the oropharyngeal microbiota of CVID showed lower alpha- and beta-diversity despite a relatively increased abundance of the order of *Lactobacillales* including the family *Streptococcaceae*. Alpha diversity was most reduced in the subgroup with undetectable IgA levels, age >40 years and severe/moderate COPD. Having undetectable serum IgA and COPD status was associated with the enrichment of Haemophilus and with the highest levels of Streptococcus, independently from recent antibiotic use. The high dysbiosis index was more pronounced in patients with COPD.

Conclusion: Adults living with CVID showed a severely reduced diversity in the respiratory microbiota with enrichment with potentially pathogenic bacteria. Our findings highlight IgA and lung damage as a potential drivers of upper respiratory tract microbiota homeostasis.



Conflicts of interest: The authors did not specify any links of interest.

000933 | Initial results from a Phase 1 single ascending dose clinical trial of STAR-0215, an investigational long-acting monoclonal antibody plasma kallikrein inhibitor for hereditary angioedema (HAE), in healthy subjects followed for at least 3 months

C. Morabito[1]; C. Stevens[2]; JK. Chung[3]; M. Gunsior[3]; K. Bernard[3]; P. Gustafson[2]; P. Bista[3]; M. Magill[2]; A. Nichols[3]; W. Lumry[4]
[1]*Astria Therapeutics, Boston, France;* [2]*n/a, Boston, USA;* [3]*Astria Therapeutics, Boston, USA;* [4]*Allergy & Asthma Specialists of Dallas, Dallas, USA*
*Presenting author: W. Lumry

Background: HAE caused by C1-INH deficiency results in uncontrolled activation of plasma kallikrein that initiates potentially life-threatening HAE attacks. STAR-0215 is an investigational humanized YTE-modified IgG1kappa monoclonal antibody with potent and durable (≥3 month) reduction of plasma kallikrein activity demonstrated in cynomolgus monkeys. This Phase 1 trial (NCT05477160) in healthy subjects is assessing whether STAR-0215 achieves potential for safe and durable suppression of HAE attacks for ≥3 months after single doses.

Method: This is a Phase 1 randomized, blinded, placebo-controlled, single ascending dose trial evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and anti-drug antibody (ADA) formation after subcutaneous (SC) STAR-0215 doses of 100 mg, 300 mg, 600 mg, or placebo in 3 cohorts (3:1 randomization) of healthy adult (18–60 years) subjects. To assess PD, plasma kallikrein activity is measured by change-from-baseline in cleaved high-molecular-weight kininogen (cHMWK). The duration of the follow-up period is 224 days; this initial report is a Day 84 unblinded interim analysis of safety, PK, PD, and ADA in these dose cohorts.

Results: 19 subjects received STAR-0215 and 6 received placebo. Related treatment emergent adverse events (TEAEs) were seen in 8 subjects (STAR-0215 n = 7; placebo n = 1) and were mild in severity. The most common TEAEs were injection site reactions (n = 6, all STAR-0215), most often erythema. STAR-0215 demonstrated dose-dependent PK, rapid absorption with an average T_{max} between 6 and 13 days and an estimated $t_{1/2}$ up to 117 days. At Day 84, mean concentrations remained above 80 nM (threshold for potential efficacy) after 300 mg and 3x over 80 nM after 600 mg. Suppression of cHMWK to levels consistent with robust plasma kallikrein inhibition was achieved through Day 84. No treatment-emergent ADAs have been detected.

Conclusion: With rapid absorption and an estimated $t_{1/2}$ up to 117 days, STAR-0215 has a favorable safety profile and robustly inhibits plasma kallikrein for at least 84 days (approximately 3 months) after a single subcutaneous dose administration in healthy subjects. These results demonstrate early proof of concept as a potential long-acting preventative therapy for HAE. Continued investigations in patients living with HAE are warranted.

Conflicts of interest: Full time employee of Astria Therpeutics.

001103 | Design of ALPHA-STAR, a phase 1B/2 proof-of-concept trial of STAR-0215 as a long-active preventative therapy in patients with hereditary angioedema (HAE) types I OR

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*Presenting author: M. Maurer

Background: HAE caused by C1-INH deficiency results in uncontrolled activation of plasma kallikrein that initiates potentially life-threatening HAE attacks. STAR-0215 is an investigational humanized YTE-modified IgG1kappa monoclonal antibody with an estimated half-life of 117 days and potent and durable (at least 84 days) reduction of plasma kallikrein activity demonstrated in healthy adult subjects. ALPHA-STAR is the first in-patient trial of STAR-0215.

Method: ALPHA-STAR (Astria Long-Acting Prophylaxis for Hereditary Angioedema-STAR-0215) is a global, multi-center Phase 1b/2 open-label POC trial in people with C1-INH HAE (types I or II). HAE patients with ≥4 HAE attacks in the prior 12 months and not receiving preventative therapy at the time of screening may enter an 8-week run-in period that will establish baseline HAE attack rate. Participants who have ≥2 attacks in the run-in may receive one dose (450 mg subcutaneously (SC), $n = 4$) or two doses (600 mg SC followed by 300 mg 3 months later, $n \leq 14$) of STAR-0215. Participants will be followed for changes in safety, HAE attack rates, pharmacokinetics, pharmacodynamics (PD), and Angioedema-Quality of Life for 6 months (168 days) after the last dose. PD will be evaluated by measuring changes in cleaved high molecular weight kininogen.

Results: Results from this POC trial will determine whether STAR-0215 may reduce HAE attacks for at least 3 months (84 days) with a favorable safety profile. Single doses of 450 mg and 600 mg are expected to produce mean concentrations at least 1.5x above the threshold predicted for HAE attack suppression through 84 days and result in robust plasma kallikrein inhibition. In addition, this trial will inform dose selection for Ph 3, including the loading dose, and will assess the effects of 300 mg as a potential maintenance dose. Durability of effects will also be assessed out to 6 months after the last dose.

Conclusion: Results from this trial will be used to determine the potential safety, tolerability, and efficacy of STAR-0215 as a long-acting preventative therapy for HAE and to plan for future clinical development.

Conflicts of interest: Full time employee of Astria Therapeutics.

001124 | Gastrointestinal system involvement in patients with primary immune deficiency

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Background: The gastrointestinal tract (GIS) is the second most commonly affected system in patients with primary immunodeficiencies (PID) and also GIS disease may be an early indicator of immune deficiency. In addition; autoimmunity, autoinflammatory, and malignancy-related GIS disorders may occur during PID follow-up. In this study, we aimed to evaluate the GIS symptoms and also endoscopic and histopathological findings of patients followed up with the diagnosis of PID.

Method: Patients who followed up with the diagnosis of PID in the Department of Pediatric Immunology and Allergy, Selcuk University Faculty of Medicine, between 2011 and 2021, were included in this study. Patients were classified according to the International Union of Immunological Societies (IUIS) for PID. We retrospectively recorded the patients' demographic data, growth parameters, and endoscopic and histopathological findings.

Results: We included 102 (56% male) patients who followed up with the diagnosis of PID. The median age at presentation was 24 months (interquartile range: 67–72 months). Consanguineous marriage was present in 44% of the patients. Primary antibody deficiency (PAD) (46%) was the most common group in PID. GIS findings were detected in 46 (45.1%) of the patients. Chronic diarrhea and growth retardation were the most common symptoms. The endoscopy process was performed in 12 of the patients with GIS symptoms. The most common histopathological finding was colitis. One patient had Trichohepatoenteric syndrome, one had congenital glycosylation defect type 1a, one had GATA-2 defect, one had chronic granulomatous disease, and three had primary antibody deficiency. Pangastritis accompanied the patients diagnosed with DiGeorge syndrome and primary antibody deficiency. A patient was diagnosed with PAD had ulcerative colitis.

Conclusion: While patients with PID may initially present with GIS symptoms, GIS findings may develop during their follow-up. Regardless of classification, patients with early-onset and atypical GIS symptoms should be evaluated for PID.

Conflicts of interest: The authors did not specify any links of interest.

000164 | **Treatment of angioedema due to acquired C1-inhibitor deficiency with PHA121, a novel oral bradykinin B2 receptor antagonist**

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Background: Acquired C1-inhibitor deficiency (AAE-C1INH) is a very rare condition caused by increased clearance or consumption of C1-inhibitor. This leads to insufficient inhibition of the contact-activation and kallikrein/kinin pathway resulting in excessive bradykinin production manifesting as angioedema attacks. Blockage of the bradykinin receptor with the subcutaneous bradykinin B2 receptor antagonist icatibant is an effective way to treat angioedema attacks in AAE-C1INH. PHA121 is a highly potent, selective, and orally bioavailable competitive antagonist of the bradykinin B2 receptor. In this proof-of-concept study we evaluated efficacy and safety of PHA121 as softgel capsule formulation (PHVS416) for on demand treatment for AAE-C1INH angioedema.

Method: A double-blind, placebo-controlled, randomized, crossover trial was conducted. Informed consent was obtained. Patients with AAE-C1INH who continued to have angioedema attacks despite curative treatment with rituximab (with or without cyclophosphamide) were eligible. Four consecutive angioedema attacks were treated with three single doses of PHVS416 (10, 20, and 30 mg) and one single dose of placebo in a randomized and blinded order. Patient-reported outcome measures were collected until 48 hours post-treatment. The primary study outcome was the change of the 3-symptom composite visual analogue scale (VAS-3) score from pre-treatment to four hours post-treatment. Safety endpoints were the occurrence of treatment-related adverse events and clinically significant changes in laboratory tests, vital signs, and ECG.

Results: A total of four patients were screened, of whom one met the eligibility criteria and completed the study. The change in VAS-3 score at four hours was +34 in the attack treated with placebo compared to −49, −10, and −27 in the attacks treated with PHVS416 10, 20, and 30 mg, respectively (Table 1 and Figure 1). Rescue medication (icatibant) was only used for the attack treated with placebo. No treatment-related adverse events were reported.

Conclusion: In this proof-of-concept study in a patient with AAE-C1INH, on demand treatment with PHVS416 was well tolerated and effectively reduced attacks symptoms compared to placebo.

	Placebo	10 mg PHVS416	20 mg PHVS416	30 mg PHVS416
Attack location	Cutaneous, facial and internal head (mouth corner)	Abdominal and cutaneous	Cutaneous	Facial
VAS-3 at pre-treatment	42	50	40	62
ΔVAS-3 at 4 hours	+34	-49	-10	-27
Use of rescue medication	Yes	No	No	No

TABLE 1. Attack characteristics, change in 3-symptom composite visual analogue scale (VAS-3) score after treatment with placebo and three different doses of PHVS416 and use of rescue medication.

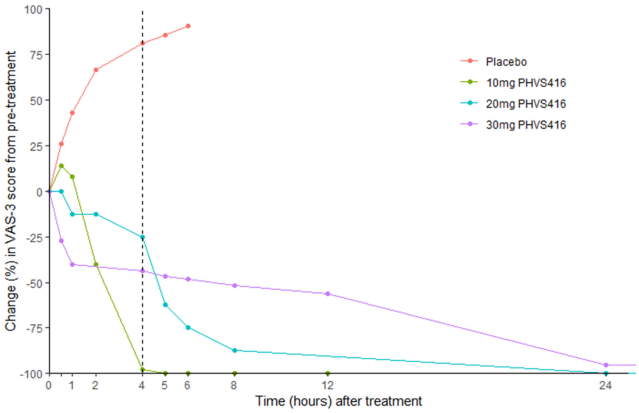

FIGURE 1. Change (%) in 3-symptom composite visual analogue scale (VAS-3) score after treatment with placebo and three different doses of PHVS416.

Conflicts of interest: This study was partially funded by Pharvaris. D.M.C. reports consultancy fees from BioCryst Pharmaceuticals, CSL Behring, Ionis pharmaceuticals, KalVista pharmaceuticals, Pharming Technologies, Pharvaris and Takeda. D.M.C. reports speaking fees from CSL Behring, Ionis pharmaceuticals and Takeda. D.M.C. reports financial research support from Ionis pharmaceuticals, KalVista pharmaceutical and Pharvaris. L.M.F. reports a travel grand from Ionis pharmaceuticals. R.S.P. declares no conflicts of interest.

Flash talks on drug allergy II

000712 | **The largest cohort of patients with hypersensitivity reactions to iron salts: Desensitization is successful in immediate reactions**

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Background: Characteristics of HSRs to iron preparations and desensitization are unknown. Therefore, we aimed to evaluate the

features of the patients with HSRs to iron agents and to assess the desensitization protocol with iron medication.

Method: We screened the medical records of 95 patients who applied to our adult allergy outpatient clinic with a history of HSRs to any iron preparations. Features of the patients and the reactions as well as the results of diagnostic skin and provocation tests were evaluated. Furthermore, we assessed the safety and success of the desensitization to iron medication, in selected cases. 2 of the 95 cases had non-immediate HSRs, one of which was a fixed drug eruption and the other was a maculopapular exanthema. The features of the remaining 93 cases with immediate HSRs were analyzed.

Results: The mean age of the patients was 39 ± 13 years and 94.7% of the patients were female. Forty-six patients had a history of HSRs to oral irons including ferrous sulfate (58.7%), ferric polymaltose complex (43.5%), and ferrous fumarate (13%) while 47 patients had a history of HRs to IV irons such as iron carboxymaltose (74.5%) and iron sucrose (31.9%). The frequency of anaphylaxis was 68.1%. Skin prick tests (SPTs) with suspected and/or alternative oral iron salts were performed in 49.5% of the patients and 5 of them were positive. SPTs and intradermal tests (IDTs) with IV iron products were applied to 65.6% and 63.5% of the patients respectively and 4 of them yielded positivity. Drug provocation tests with the culprit and alternative irons were performed in 40.9% and 34.4% respectively. Ten and 31 patients had asthma and a history of previous HSRs to other drugs respectively. Eighteen patients were using a proton pump inhibitor concomitantly. Anaphylaxis was more common in patients hypersensitive to IV agents than the oral ones ($p < 0.001$). In selected 17 cases for whom iron agents were mandatory, 55 successful desensitization in repeated usage were performed. In eleven cases, the diagnosis was proven with DPTs while the remaining 7 patients considered high risky due to severe index reactions in history.

Conclusion: Our study indicated that skin tests are not helpful in the diagnosis of HSRs to iron products and parenteral route of administration is related to severe HRs. Furthermore, in case of necessity, our IV desensitization protocol generated for carboxymaltose is a safe and practical treatment of choice.

Conflicts of interest: The authors did not specify any links of interest.

000739 | Evolution of nonimmediate hipersensitivity to betalactams in children

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Background: The natural history of Betalactams (BLs) allergy remains unknown. However, few studies suggested that children diagnosed with nonimmediate-hypersensitivity-reactions to BLs (BLs-NIR) may tolerate subsequent treatments with these antibiotics. Our aim was to evaluate the evolution of BLs-NIR in children.

Method: A prospective study was carried out evaluating children (<16 y.o) diagnosed of BLs-NIR by a positive initial drug provocation test (iDPT) in our allergic unit between 2010 and 2020. All patients included presented mild-NIR in the iDPT. Rechallenge, without previous skin testing, was performed with the culprit BL at least after 1 year of the diagnose. Atopy was assessed by prick test with a panel of common aeroallergens.

Results: A total of 16 children with positive iDPT were included (62.5%males). The 62.5% were sensitized to aeroallergens (43.5% polysensitized, 6.3% mites, 6.3% cat/dog dander, 6.3% pollen). Concerning other allergic diseases, the 81.3% present atopic dermatitis(AD), 37.5% rhinoconjunctivitis (RC), 18,8% asthma and 6.3% food allergy.

Regarding the culprit BL, amoxicillin was involved in 75% and amoxicillin-clavulanic acid in 25%. The symptoms presented in the iDPT were: urticaria/AE in 11 and maculopapular exanthema (MPE) in 5. The mean time between the iDPT and rechallenge was 6.7 years (QIR: 4.8–8.1). Rechallenge was negative in 10 (62.5%) patients, and positive in 6 (37.5%): 4 presented urticaria/AE and 2MPE. Within the positive group, the time-interval between the onset of symptoms after the drug-rechallenge was <24h in 1 child, and ≥ 3 days in 5.

Comparing both groups, statistical differences were observed in AD, being more frequent in allergic ($p = 0.036$). No differences were observed for age, gender, atopy, other allergic diseases, culprit BL, clinical entities in iDPT or time between iDPT and rechallenge. Although no significant, the mean age at iDPT was lower in the negative group (4.5 vs 8.4 y.o) ($p = 0.084$).

Conclusion: Less than a half of children included in our study remained allergic in the re-evaluation, being mild all the reactions presented in the rechallenge. In most cases a prolonged challenge at home was necessary for establishing the diagnose.

P	G	Age at iDPT (y.o)	Culprit BL	iDPT (clin entity)	Time between iDPT and rechallenge (years)	Rechallenge (clin entity)	TI (days)
1	F	4	AX	URT	12	URT	3
2	M	11	AX-CLA	MPE	11	URT	7
3	M	16	AX-CLA	URT/AE	10	MPE	3
4	M	6	AX	MPE	8	(-)	
5	F	14	AX-CLA	URT	4	(-)	
6	M	5	AX	MPE	4	MPE	4
7	F	8	AX-CLA	AE	2	AE	1 (7h)
8	M	2	AX	MPE	6	(-)	
9	M	2	AX	URT/AE	7	(-)	
10	M	3	AX	URT	3	(-)	
11	M	3	AX	MPE	6	(-)	
12	F	1	AX	URT/AE	6	(-)	
13	M	7	AX	URT	7	URT	7
14	M	9	AX	URT	6	(-)	
15	F	4	AX	URT	8	(-)	
16	F	1	AX	URT	8	(-)	

Abbreviations: P: patients, AX: amoxicillin; AX-CLA: amoxicillin-clavulanic acid, iDPT: initial drug provocation test, G: gender, M: male, F: female, MPE: Maculopapular exanthema, URT: Urticaria, AE: angioedema, TI: time interval from drug administration to reactions. Clin entity: clinical entity.

Conflicts of interest: The authors did not specify any links of interest.

000689 | Hypersensitivity reactions to antibiotics in mastocytosis – Prevalence and clinical features

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Background: Anaphylactic reactions are a well-known clinical feature of patients with mastocytosis and a strong association between patients with venom-induced anaphylaxis or unprovoked anaphylaxis and mastocytosis have been established. Although data on the frequency of drug hypersensitivity reactions in mastocytosis is limited, it is hypothesized that these patients may even predispose systemic hypersensitivity reactions to certain drugs including antibiotics. Nevertheless, this issue has not been systematically investigated. Hence, in the current study, we aimed to investigate the actual prevalence and clinical features of antibiotic-related hypersensitivity reactions in patients with mastocytosis.

Method: A 15-year retrospective study was conducted among 239 (≥ 18 years old) consecutive patients with mastocytosis who were investigated in the Mastocytosis Center Karolinska. Of patients, 192 received diagnosis of mastocytosis, whereas remaining 47 obtained diagnosis of monoclonal mast cell activation syndrome (MMAS). All patients underwent a thorough allergy work-up where self-reported antibiotic hypersensitivity reactions were assessed for each individual patient by an allergist.

Results: Overall, 34 patients (14.2%) were deemed to have a hypersensitivity reaction to antibiotics Moreover, these patients had a total of 38 reactions, as four patients reacted against two different antibiotics. Frequency of antibiotic hypersensitivity were similar among patients with mastocytosis and MMAS. Most patients reacted with cutaneous symptoms (74%), as pruritus being the most frequent symptom (29%). Overall prevalence of anaphylaxis was 0.8% and confirmed only in two of 34 patients with antibiotic hypersensitivity (5%). Beta-lactams were the most common elicitors (63%) and all antibiotic-related hypersensitivity reactions were experienced before mastocytosis were diagnosed. There were no differences in age, gender, bone-marrow findings, atopic status and tryptase levels between mastocytosis patients with and without antibiotic hypersensitivity.

Conclusion: The prevalence of antibiotic hypersensitivity is found to be 14.2% in our mastocytosis cohort, which is similar to those of the general population. Hence, our results suggest that mastocytosis patients without history of hypersensitivity reactions to antibiotics may be treated with these drugs without special precautions.

Conflicts of interest: The authors did not specify any links of interest.

001015 | Perioperative allergic reaction to patent blue – A case series

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Background: Anaphylaxis is a constant perioperative concern due to possible hypersensitivity reactions to several agents. Patent Blue dye V(PBV) is estimated to be responsible for 0.6% of reported anaphylactic conditions. We report 9 patients assessed in our department with suspected PBV allergic reactions.

Method: Retrospective study of patients with confirmed or suspected PBV reaction. Demographic and clinical data were obtained from clinical records.

Results: Nine female patients, mean age 53 years [40–80], received PBV to identify sentinel lymph node involvement in breast cancer surgery. Onset of symptoms occurred within 15 minutes of PBV exposure for 8 patients and a delay of 60 minutes for 1 patient. Six reactions were Grade 3, two Grade 2, and one Grade 1. All patients received intravenous crystalloid, clemastine and hydrocortisone. Adrenaline was administered to seven patients. Four patients required critical care admission.

Clinical reaction: hypotension n = 6; blue wheals n = 4; angioedema=3; urticaria n = 2; laryngeal oedema, bronchospasm and/or cyanosis n = 1.

Baseline tryptase serum level was determined for 3 of the patients with normal values (2.4, 5.3 and 7.4 ug/L). At the time of reaction, tryptase serum level was available for only one patient with a significant increase compared to the baseline value (200 vs 5.3ug/L).

During diagnostic investigation, negative skin test results were obtained for all specific drugs used in each case (midazolam, fentanyl/remifentanil, rocuronium, propofol, atropine, esomeprazole, ondansetron, dexamethasone, tramadol, metamizole, ketorolac), including latex, iodopovidone and chlorohexidine. Negative beta-lactam skin tests and cefazoline challenge tests were obtained from patients that received cefazoline prophylactically.

PBV skin tests were positive for 8 patients: skin prick tests(SPT) 1:1 (25 mg/mL) n = 2; intradermal tests(IDT) 1:100000 (0.00025 mg/mL) n = 4; IDT 1:100 (0.25 mg/mL) n = 2. Basophil activation test (BAT) was performed in 3 patients with a positive result in two cases. For one patient, despite the severe reaction with hypotension and blue wheals suggesting PBV reaction, negative SPT/IDT and negative BAT test for PBV didn't allow to conclude about the identification of the culprit.

Conclusion: Identifying the agent responsible for anaphylaxis in patients under general anesthesia is often difficult, but crucial to preventing future events. Surgeons and anesthetists who use patent

blue dye should be informed to the risk of allergic reactions to this dye.

Conflicts of interest: The authors did not specify any links of interest.

001179 | Diagnostic clinical clues in actual NSAID hypersensitivity in pediatric patients

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used in childhood due to their anti-inflammatory and antipyretic effects. Thus, this group of drugs including ibuprofen and paracetamol are frequently associated with hypersensitivity reactions. The aim of this study is to reveal the actual frequency of NSAID-hypersensitivity (NSAID-H) and to determine the risk factors in pediatric age.

Method: 189 suspected NSAID-H reactions were examined in 134 pediatric patients referred to Istanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital Pediatric Allergy outpatient clinic between 01 September 2017 and 15 February 2021. Demographic and clinical features of the patients as well the results of diagnostic tests with the culprit NSAID and aspirin (in order to reveal cross-reactivity) were recorded for each patient.

Results: 126 of 134 pediatric patients [6.8 (3.8–12) years, 59% male] and 180 of 189 suspected NSAID-H reactions were evaluated diagnostically. As a result of diagnostic tests actual NSAID-H was detected in 33 of 126 patients (26.1%) and in 45 of 180 suspected reactions (25%) and the cross-reactivity was established in 72% of the NSAID-hypersensitive patients. Considering all the clinical variables during the reaction; multivariate logistic regression analysis revealed that a suspected reaction occurring in one hour after the NSAID intake (OR: 3.1 95%CI: 1.03–9.90), emergence of isolated facial angioedema (without urticaria) during the suspected reaction (OR: 8.5 95%CI: 2.96–24.55) and a reaction due to a NSAID other than paracetamol or ibuprofen (OR: 10.2 95%CI: 2.89–36.08) increased the risk of actual NSAID-H, ($p < 0.05$ for all). All these three variables together predicted an actual diagnosis of NSAID-H with a positive predictive value, negative predictive value, sensitivity and specificity of 88%, 78%, 21.2%, 99% respectively with an accuracy of 80% and an area under curve of 0.600.

Conclusion: NSAID-H was detected in nearly one fourth of the patients referred due to a suspected NSAID-H reaction. A suspected reaction occurring in one hour after the NSAID intake, emergence of isolated facial angioedema (without urticaria) during the suspected reaction and a reaction due to a NSAID other than paracetamol or ibuprofen increased the risk of actual NSAID-H, and would be important predictive clues in the diagnosis of actual NSAID-Hypersensitivity.

Conflicts of interest: The authors did not specify any links of interest.

001356 | Novel targeted-inhibition of the il-5 axis for drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome

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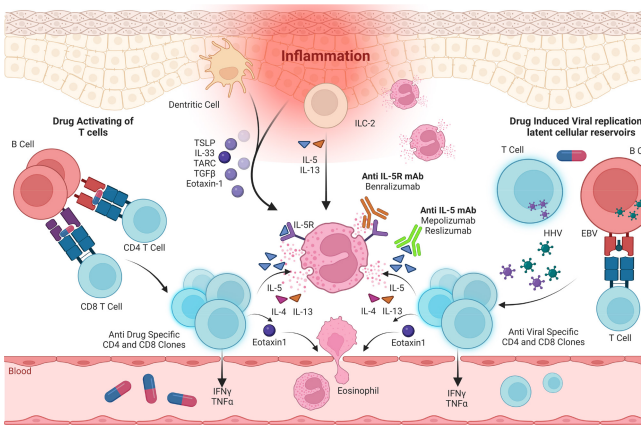
Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome represents a severe hypersensitivity reaction. Up-to-date treatment is based on withdrawal of medication, supportive care, and immunosuppression using high-dose corticosteroid (CS) therapy. However, evidence-based data are lacking regarding second-line therapy for steroid-resistant or steroid-dependent patients.

Method: We hypothesize that the interleukin-5 (IL-5) axis plays a critical role in the pathophysiology of DRESS, and hence inhibition of this signaling pathway could offer a potential therapy for steroid-depended and/or steroid-resistant cases and it may offer an alternative to CS therapy in certain patients more prone to CS toxicity.

Methods: Herein we present two cases of DRESS and preformed a literature review of all DRESS cases treated with biological agents targeting the IL-5 axis, indexed in PubMed up to Oct. 2022.

Results: Thirteen patients received IL-5 targeted therapy for DRESS, with a slight female predominance of 61% (8/13) and a mean age of 56 years old. Mepolizumab was administered to five patients, one patient was treated with reslizumab, six patients were treated with benralizumab and one patient received benralizumab followed by mepolizumab therapy. All patients received concurrent corticosteroid therapy, two cases received additional therapy with intravenous immunoglobulin and one patient received concurrent therapy with cyclosporine and cyclophosphamide. The clinical indication for initiation of anti-IL5 targeted therapy was due to steroid-resistant DRESS in eight patients, steroid-dependent and relapsing cases in three patients, one patient received upfront therapy to avoid GC toxicity, and one patient as part of desensitization, to continue the culprit drug. Anti-IL-5 treatment regimen differed: six patients received a single dose, and seven patients required multiple doses. However, all cases responded with complete resolution of DRESS symptoms, laboratory recovery, and complete weaning off from steroid therapy.

Conclusion: Future implementation of IL-5 axis blockade could offer a steroid-sparing effect, potential therapy to steroid-resistant cases, and perhaps offer an alternative to CS in certain DRESS patients more prone to CS toxicity.



Conflicts of interest: The authors did not specify any links of interest.

000765 | Successful desensitization to gonadotropin-releasing hormone analogue (triptorelin)

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Background: Gonadotropin-releasing hormone (GnRH-α) analogues are prescribed in patients with endometriosis to induce an hypoestrogenic state for the ameliorating of pain. Triptorelin is one of the most widely used GnRH-a. Hypersensitivity reactions to GnRH analogues is very uncommon and there are not drug desensitization protocols described in the literature.

Method: A 40-year-old woman diagnosed with endometriosis was being treated with monthly intramuscular (IM) triptorelin acetate for the treatment of the pain. After three months of treatment with a dose of 3.75 mg/month, she began to present moderate lip edema in the first 30 minutes after its application, she denied other symptoms. The edema resolved with corticosteroids and antihistamines. She was evaluated by allergology. An intradermal test was performed, being strongly positive. The patient was diagnosed with triptorelin allergy and because of the need of the drug administration, it was decided to carry out a triptorelin desensitization. The protocol to depot triptorelin acetate (Decapeptyl 3.75 mg/mL) was designed in 6 steps, with 20-minute intervals, reaching a maximum dose of 3.75 mg, over a period of 6 hours. During the first desensitization, she presented lower lip edema 30 minutes after the last infusion, that resolved with the administration of cetirizine. Subsequently, monthly doses of IM triptorelin acetate was administered under the same regimen, with cetirizine and acetaminophen premedication, with adequate tolerance.

Results: We obtain all the information from the record and patient itself. The intradermal was performed using 0.1 cc of the original 3.75 mg ampoule in 2 ml of normal saline (concentration of 0.1875 mg). Desensitization was made in the allergology unit. On each step it was given the next doses: On step 1- 0.1 mg, step 2- 0.37 mg, step 3- 0.56 mg, step 4- 0.74 mg, step 5- 0.93 mg and step 6- 0.93 mg reaching the total dose of 3.75 mg, under the constant supervision of vital signs and the physician in charge of the patient.

Conclusion: We report a case of successful desensitization to triptorelin in a patient with a proven allergy to this drug. A 6-step desensitization protocol was used to allow her to continue receiving in a safe way the optimal medical therapy.

Conflicts of interest: The authors did not specify any links of interest.

000310 | No evidence of isotretinoin sensitisation in peanut allergic children

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*Presenting author: J. Hourihane

Background: Background: Isotretinoin is an oral medication for severe nodular cystic acne. The summary of product characteristics (SPC) for isotretinoin capsules includes refined soya bean oil as an excipient. The manufacturers state that, as a result, isotretinoin is contraindicated in patients with soya and/or peanut allergy. This SPC warning limits treatment options for peanut allergic patients with acne. Allergists consider it highly unlikely that patients with peanut allergy would develop a cross reactive allergy to isotretinoin. However recent publications propose peanut allergic subjects should have their first dose of isotretinoin in an observed setting, or undergo soya allergy testing before isotretinoin initiation. This is despite clear evidence of very little clinical allergic cross reactivity between soya and peanut and that refined oils (such as peanut oil) do not induce allergic reactions.

Method: To determine the prevalence of sensitisation to isotretinoin in peanut allergic children, as measured by skin prick test (SPT). If 59 consecutive subjects did not show a positive SPT there is 95% probability that the chance of reaction to isotretinoin is <5% (log 0.05/log 0.95 = 58). Because isotretinoin is considered potentially teratogenic in females, only male children were studied and only male staff or female staff with completed families were involved. All cases underwent isotretinoin prick-to-prick skin prick testing using an opened capsule. A skin prick test wheal diameter of >3 mm was considered positive.

Results: Results: 69 cases were recruited, 3 were excluded (1 negative peanut SPT, 1 SPT of 7mm but had not eaten peanut, 1 was a duplication). 66 were included for analysis; mean age 11 years (range 3–19 years). Peanut allergy was confirmed in 60 – consistent history and positive peanut SPT, and suspected in 6 – not currently consuming peanut but peanut SPT [3]8 mm- mean 10mm (range 8–14 mm). No subject had a positive SPT to isotretinoin.

Conclusion: There was no documented isotretinoin sensitisation in a study adequately powered to suggest it is very unlikely in the wider peanut allergic population. This suggests steps should be taken to

change the SPC sheet for isotretinoin, to allow dermatologists to use it in all their patients and to remove an unjustified barrier to health care for peanut allergic teenagers with acne.

Conflicts of interest: The authors did not specify any links of interest.

001434 | Observational study of changes in B cells, BREG cells and amoxicillin-specific immunoglobulins after a type-I hypersensitivity reaction in allergic patients to amoxicillin

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Background: Immediate drug hypersensitivity reactions (IDHRs) to betalactams (BLs), especially those triggered by amoxicillin (AX), are increasing over recent years. During the sensitisation phase, B cells produce a high amount of specific immunoglobulin E (sIgE), which couples to the high-affinity receptors of basophils and mast cells. After the re-exposure to the drug, these cells degranulate, releasing proinflammatory mediators and cytokines. Little is known about how different immunoglobulins, B cells subsets, and B regulatory (Bregs) cells change over time after the reaction. In this study, we aimed to analyse both humoral and cellular B cell responses in patients with IDHRs to AX at different timepoints after the acute reaction.

Method: Blood and serum samples were obtained from 20 selective allergic patients to AX, and from 10 healthy controls. Samples from AX-allergic patients were obtained at different timepoints from the acute reaction (<6, 6–12, 12–24, >24 months). Serum AX-sIgE was measured by radioallergosorbent test (RAST) and ImmunoCAP; serum AX-sIgG and -sIgG4 by immunoCAP; and other different AX-sIgG subclasses by ELISA. Peripheral blood mononuclear cells (PBMCs) were isolated and the frequencies of B cells expressing BCRs of different immunoglobulin heavy chain isotypes as well as Breg cells were analysed by flow cytometry.

Results: Higher serum-sIgE levels were observed in samples from allergic patients of <6 months after the reaction, which showed a significant decrease after 6 months. In contrast, AX-sIgG was reduced during the first 12 months compared to after 12 months from the reaction. This increase was also observed in AX-IgG2, while AX-IgG3 seemed to decrease over time. The frequencies of $IgA1^+$ and $IgA2^+$ B cells, were increased between 6 and 24 months from the reaction. Interestingly, frequency of $IgG2^+$ B cells increased between 12 and 24 months, while $IgG4^+$ B cells increased significantly between 6 and 12 months, decreasing again after 12 months. The frequencies of plasmablasts, B10, and Br1 cells producers of IL-10 or which express IL1Ra was significantly reduced in samples of <6 months after the reaction, although slowly increased over time since the reaction.

Conclusion: Serum AX-sIgE was closely related to the acute phase of the IDHR, whereas AX-sIgG, and concretely IgG2 and IgG4 seem to have a protective role, as it has been shown at humoral and cellular levels. The reduced frequency of $IL10^+$ and $IL1Ra^+$ plasmablasts, B10, and Br1 cells in the first months after the reaction seems to be relevant during the first steps of IDHRs to AX.

Conflicts of interest: The authors did not specify any links of interest.

000690 | Evaluation of hypersensitivity reactions in children with rheumatologic diseases during treatment with biological agents

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Background: Biological agents (BA) such as growth factors, immunomodulators, monoclonal antibodies (mAbs), and vaccines are currently used to treat autoimmune, autoinflammatory, and malignant diseases. Hypersensitivity reactions (HR) to these drugs are becoming more common due to their increasing use. The excipients, particularly polyethylene glycol and polysorbate in intramuscular and/or intravenous formulations, are also responsible for many drug allergies. It is not always clear whether the primary molecule or the excipients are responsible for HR. The aim of this study was to assess the frequency and characteristics of such reactions in pediatric patients taking biologics for the treatment of rheumatologic diseases and also to evaluate polysorbate and polyethylene glycol sensitization in patients who develop HR to biologics, including PEG or polysorbate derivatives.

Method: Medical records of pediatric patients treated with biologic agents in our Division of Pediatric Rheumatology were reviewed, and adverse events were retrospectively evaluated. We also performed skin tests and basophil activation tests (BAT) or patch tests in patients with a history of HR, depending on the type of reaction.

Results: Six hundred twenty-one children with juvenile idiopathic arthritis, familial Mediterranean fever, vasculitis, and other diseases using various BA were studied. Patients who experienced an adverse event were categorized at BA. Reactions were divided into four categories: Type 1 reactions, cytokine release reactions, infusion-related/delayed immunoglobulin reactions, and T-cell-mediated reactions. The severity of the reaction was graded according to the Brown classification. In the patients with type 1 reactions, skin and basophil activation tests were performed. In patients with delayed-type HR reactions, a patch test was performed. Desensitization to the causative drug was performed in one patient with HR, while the other patients continued treatment with premedication or switched to other drugs.

Conclusion: Experience with hypersensitivity reactions to BD in children is sparse compared with series in adults. As the use of BD increases in pediatric patients, life-threatening drug HRs will

become more common, and prospective studies on this topic will provide more data in the future.

Conflicts of interest: The authors did not specify any links of interest.

000212 | Negative predictive value of provocation tests with beta-lactams in children: A single-center's experience

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Background: Beta-lactam antibiotics (BLA) are one of the most prevalent causes of drug hypersensitivity reactions in children. The drug provocation test (DPT) is the gold standard for identifying suspected immediate and nonimmediate reactions. Our main aim was to evaluate the frequency of confirmed immediate and nonimmediate reactions to BLA, and as well as the negative predictive value (NPV).

Method: Over a 5-year period, children diagnosed with immediate and nonimmediate type BLA hypersensitivity in our Allergy Unit were included in this retrospective study. Immediate reactions were classified as those that occurred within 1 hour of drug exposure, whereas nonimmediate reactions occurred more than 1 hour later. During the following procedures, all pediatric patients with suspected immediate or nonimmediate reactions were only tested with the suspected drug.

Results: A total of 81 patients (46.9% girls) were included in the study. Patients were divided into two groups, according to the reported type of reaction: 37 children had a history of immediate-type reactions, and 44 had nonimmediate reactions. The median and the interval between DPT and reaction time was similar in the two groups (7 months, interquartile range [IQR] = 2–25 months, 7 months [IQR] = 2–14.75 months). The age at the time of evaluation was lower among children with nonimmediate reactions. The most common suspectible drug was amoxicillin-clavulanate in each group. DPT were positive in 14 of the 37 children (37.8%) with immediate reactions, and 6 of the 44 children (13.63%) with nonimmediate reactions. We determined a high (93.3%) negative predictive value of DPT for BLA were 93.3% and 90.9% for immediate and nonimmediate type reactions, respectively.

Conclusion: Our results suggest that the possibility of diagnosing beta-lactam allergy is higher with immediate reactions compared with non-immediate reactions. In our study, the negative predictive value of DPT was high for immediate and nonimmediate reactions. This situation showed us that unneeded drug removal should be avoided and the decision should be made with appropriate tests on a patient basis.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on genomics and proteomics

001377 | The effect of maternal probiotic supplementation on biomarkers of systemic allergic inflammation in 2-year-old children

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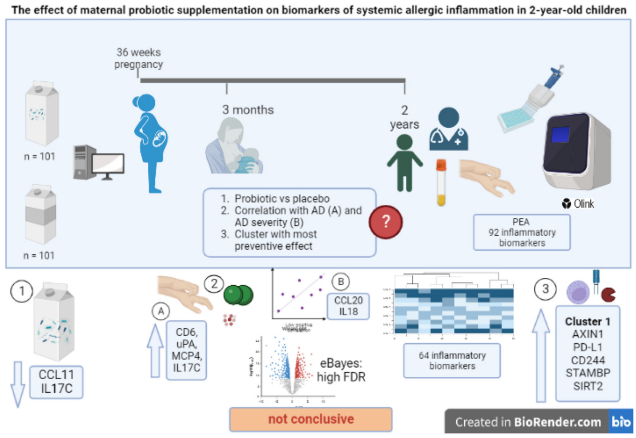
Background: Microbiota disruptions in the first months of life have been linked to the development of allergic diseases including atopic dermatitis (AD). Probiotic supplementation has a promising effect on AD prevention in infancy. We investigated whether maternal probiotics supplementation influenced plasma inflammatory biomarkers in their offspring at 2 years of age and they correlated with the presence and severity of AD. We also examined if the overall inflammatory protein profile was associated with the degree of preventive effect of probiotics.

Method: Ninety-two (92) inflammatory proteins were measured in plasma samples from 2-year-old children ($n = 202$) whose mothers had participated in a placebo-controlled randomised trial of probiotic supplementation. The mothers consumed a probiotic or placebo milk from 36 weeks gestation until 3 months after birth with the probiotic milk containing *Lactobacillus rhamnosus GG*, Bifidobacterium *animalis subsp. lactis Bb-12* and Lactobacillus *acidophilus La-5*. A multiplex proximity enhanced extension assay was used to measure the inflammatory proteins. Associations between these proteins and the presence and severity of AD, and the degree of preventive effect, was estimated individually and collectively using clustering analysis.

Results: The probiotic group had lower CCL11 and IL-17C, while children with AD had higher IL-17C, MCP-4, uPA, and CD6. Cytokine CCL20 and IL-18 had moderate correlation ($r = 0.35$) with the severity of AD. After accounting for multiple comparison however, no biomarkers were conclusively associated with maternal probiotic supplementation, or the presence and severity of AD. Cluster analysis suggested that those with the highest value of immune check receptors and inflammatory suppressor enzymes was associated with the greatest preventive effect.

Conclusion: We found no conclusive evidence that maternal probiotics influenced individual or the overall inflammatory biomarkers' profile at two years of age, nor that these proteins are associated with the presence or severity of AD. Nevertheless, the proteins associated with presence and severity of AD prior to adjusting for multiple comparisons warrant attention because of their potential biological relevance. Cluster analysis may provide a more nuanced approach in analysing subtype of probiotic responders.



Graphical Abstract for The effect of maternal probiotic supplementation on biomarkers of systemic allergic inflammation in 2-year-old children

Conflicts of interest: The authors did not specify any links of interest.

001125 | Genomic risk scores and molecular biomarkers for oral immunotherapy treatment response in children with peanut allergy

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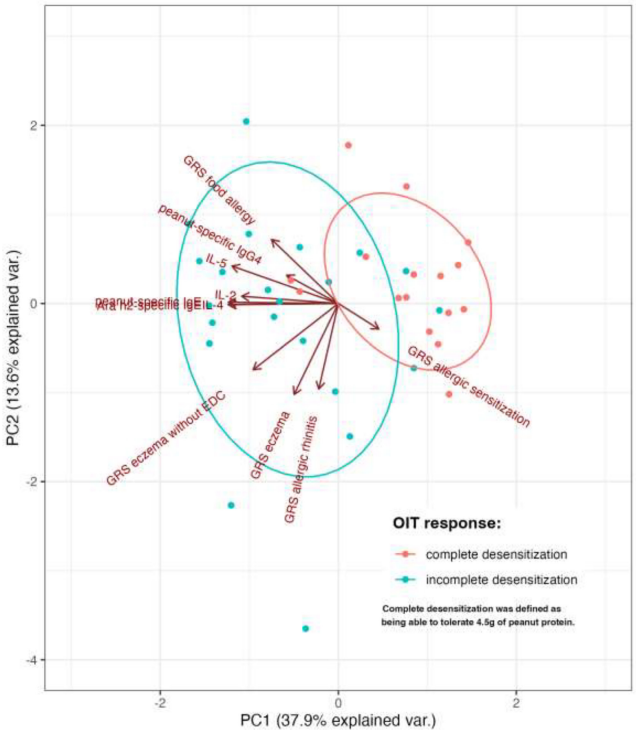
Background: Oral immunotherapy (OIT) is currently the only available alternative to strict food avoidance in children with peanut allergy (PA). Nevertheless, OIT involves a significant risk of allergic reactions including anaphylaxis. Moreover, over half of PA patients do not achieve complete desensitisation after OIT. Thus, there is a need to develop tools capable of predicting OIT response.
Method: Of 38 PA children who concluded an OIT trial, only 16 were able to tolerate 4.5 g of peanut protein after OIT (*i.e.* classified as completely desensitized). The other 22 children were incompletely desensitized. Genome-wide SNP genotypes were used to construct Genomic Risk Scores (GRS) weighted by the genetic risk of PA comorbidities (*i.e.* food allergy, eczema, asthma, allergic rhinitis and allergic sensitisation). Blood samples obtained before OIT were used to measure IL-2, IL-4, IL-5, IL-10, IFN-γ and TNF-α cytokines in cell culture supernatants, as well as Ara h2-specific IgE, peanut-specific IgE and IgG4 in serum. In this study, we used GRS alone, and in combination with cytokine and immunoglobulin levels to predict peanut OIT response.
Results: Incompletely desensitised children had significantly higher GRS for eczema, food allergy and allergic rhinitis than completely desensitised children. GRS, cytokines and immunoglobulins alone significantly explained variability in desensitisation, and up to 83.65% when combined all together. Ara h2 IgE, peanut-specific IgE, IL4 and IL5 had the best discriminative power to classify OIT outcomes alone (AUC = 0.817–0.835). Of the genetic predictors, the GRS for eczema achieved the best discriminative power (AUC = 0.778). All predictors in combination achieved an excellent power (AUC = 0.98). After principal component analysis of all significant biomarkers (*i.e.* GRS, cytokines and immunoglobulins), the 1st and 2nd principal components (PC) were able to distinguish completely from incompletely desensitized children (Figure 1).
Conclusion: GRS are a potential predictive tool to identify in advance children that may not benefit from OIT, especially when combined with other biomarkers.



Conflicts of interest: The authors did not specify any links of interest.

001663 | GEOMX™ spatially resolved transcriptomics reveals inflammatory and metabolic responses in chronic rhinosinusitis with nasal polyps following anti – IL-5 treatment

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*Presenting author: N. West

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory disease of the nasal mucosa that is largely

unresponsive to clinical management. Treatment with an anti – IL-5 treatment for six months in individuals with an eosinophilic sub-type of CRSwNP reduced sinonasal eosinophil counts and increased the concentration of type 2 cytokine concentrations. Whilst the degree of mucosal eosinophilic infiltration in CRSwNP predicts disease severity, deeper characterisation of polyp cellular and molecular diversity may improve diagnostic and therapeutic strategies. We applied targeted GeoMx™ Digital Spatial Profiling (DSP) to examine the sinonasal transcriptomic response over six months of anti – IL-5 treatment.

Method: Formalin-fixed paraffin embedded slides of sinonasal biopsies collected at pre-treatment and at four weekly intervals through to week 26 of treatment and three months after treatment with an anti-IL-5 inhibitor (Mepolizumab, GSK, UK). Slides were stained and analysed on the NanoString GeoMx™ DSP platform. Sequencing was completed on a NovaSeq 2000. Data was normalised by TMM with edgeR (v3.36) and differential expression calculated with limma (v3.50.3). Significance was considered with adjusted and unadjusted p-values.

Results: Mean age of the participants was 47.7 ±11.6 with 50% female. Changes in gene expression exhibited a U-shaped pattern, with the greatest effect of Mepolizumab on immune gene expression from pre-treatment observed at week 20 and minimal changes observed three months after treatment. Changes in key inflammatory signalling pathways included T-helper lineage commitment and negative regulation of type-2 immune responses. Comparisons between responders and non-responders showed a more significant effect across regulation of the antioxidant system and apoptosis in the in the *mTOR* and *PI3K/AKT* pathways.

Conclusion: To our knowledge, this is the first study applying spatial profiling to examine nasal polyp mucosa to discern treatment effects. Anti – IL-5 treatment exerted a sustained and increasing transcriptional response within the nasal polyp over the six months of treatment that reversed upon cessation of treatment. Changes to cell metabolism and the antioxidant system were observed, with these effects more evident in responding patients. Our results extend understanding of Mepolizumab's anti-IL-5 activity beyond inhibition of eosinophils and inflammation.

Conflicts of interest: NPW, AJC, PS, RH and RA received research funding from GSK.

000188 | Modifications in the lung DNA methylation landscape in a murine model of respiratory allergy induced by two *Blomia tropicalis* allergens

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Background: *Blomia tropicalis* is globally one of the main inductors of allergic asthma and sensitization. The epigenetic effects of house dust mites exposure to the airways are not completely investigated. Some studies have reported alterations in lung DNA methylation in mice or bronchial epithelial cells exposed to *Dermatophagoides* spp. extract. However, the epigenetic modifications induced by *B. tropicalis* extract or individual allergens are still unknown. We aimed to evaluate the lung DNA methylation landscape in mice exposed to *B. tropicalis* extract and the allergens Blo t 2 and Blo t 13.

Method: Six weeks old female BALB/c mice were intraperitoneally immunized and intranasally challenged with Blo t 2, Blo t 13, *B. tropicalis* extract, or saline solution (n = 6 mice per group) in a model of acute allergic airway inflammation. DNA methylation in over 285 000 CpG sites was evaluated using Infinium Mouse Methylation BeadChip. Beta values were converted to M values, which were used for principal component (PC) analysis and PC-adjusted linear regression for differential methylation. Transcription start sites within 250 kb of significant CpGs were used for gene annotation.

Results: DNA methylation in allergen-exposed mice clustered separately from control mice. There were 57, 7, and 42 differentially methylated CpGs (effect size ≥ |1.4| and FDR-adjusted *p*-value < 0.05) when comparing mice exposed to Blo t 2, Blo t 13, or *B. tropicalis extract* with control mice, respectively. Among the top 5 significant CpGs, some of the associated genes were: *Naalad2* and *Vps41* (Blo t 2), *Gdf7* and *Cxcl10* (Blo t 13), and *Naalad2* and *Or8g32* (*B. tropicalis* extract). Some of these genes are involved in inflammatory and remodeling pathways in the lung.

Conclusion: Our study shows for the first time that exposure to either whole extract from *B. tropicalis* or individual allergens (Blo t 2 and Blo t 13) modifies the DNA methylation landscape in the mouse lung. The implicated genes and biological pathways are important for the pathogenesis of allergic asthma and the mechanisms of the inflammatory response to inhalant allergens.

Conflicts of interest: The authors did not specify any links of interest.

000611 | Protein serum profile identification and in silico system biological analysis in patients with drug-induced anaphylaxis

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*Presenting author: E. Nuñez-Borque

Background: Anaphylaxis is the most severe manifestation of allergic disorders. This reaction can be induced by different triggers, being drugs the most frequent in adults. Currently, the diagnosis of anaphylaxis is based on the recognition of clinical symptoms, which are common to many other pathologies. Therefore, it is necessary to complement it using molecular markers. The main one employed in clinical practice is serum tryptase. However, this protein has several drawbacks since it is not elevated in most cases. Therefore, our aim was to determine the serum circulating protein profile of patients with drug-induced anaphylaxis to identify new reliable biomarkers.

Method: The circulating serum protein profile was determined by mass spectrometry (TMT-LC-MS/MS) from acute (anaphylaxis) and baseline (at least 14 days after the reaction) samples from 10 patients with severe drug-induced anaphylaxis. In turn, the three proteins with the highest fold change (ApoAII, ApoH and THBS1) were selected to validate their levels by immunodetection techniques in a larger cohort of 65 patients with drug-induced anaphylaxis, including moderate and severe reactions. Moreover, the coordinated function of the proteins identified by mass spectrometry was determined by system biology analysis (SBA).

Results: A total of 865 proteins were identified by mass spectrometry. However, only 76 of them showed significant differences between acute and basal phases. Precisely, 10 increase and 66 decrease during the reaction. Furthermore, increased levels of THSB1 and decreased levels of ApoAII and ApoH were confirmed in a larger cohort of patients with drug-induced anaphylaxis. In turn, the main signaling pathways described in SBA were inflammation, complement and coagulation, processes closely related to anaphylaxis.

Conclusion: We identify a differential circulating serum protein profile in patients with drug-induced anaphylaxis. Furthermore, we confirm an increase in THSB1 and a decrease in ApoAII and ApoH levels, proposing them as candidate biomarkers for the diagnosis of anaphylaxis.

Conflicts of interest: The authors did not specify any links of interest.

000944 | Interleukin-4-induced loss of smell in mice is associated with transcriptome and proteome changes suggestive of neuroinflammation and altered olfactory/calcium signaling

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*Presenting author: Y. Hara

Background: Dupilumab, which binds to and prevents signaling by interleukin-4 receptor alpha (IL-4Rα), the shared receptor for IL-4 and IL-13, rapidly improves sense of smell as early as Day 3 in patients with chronic rhinosinusitis with nasal polyps (CRSwNP). Recent studies in mice showed that administration of IL-4, but not IL-13, induces rapid loss of smell, by Day 5, suggesting that IL-4-signaling effects play a dominant role in the restoration of smell with dupilumab. The current study aimed to further define the pathophysiological mechanisms of IL-4-evoked loss of smell in mice using transcriptomic and proteomic profiling.

Method: Male BALB/cJ mice received intranasal administration of IL-4 and/or IL-13 daily for 5 days (Days 0–4). IL-4Rα antibody (dupilumab surrogate) was injected intraperitoneally on Days −3, 0, and 3. After treatments, the olfactory epithelium was dissected and subjected to RNA extraction for transcriptomic profiling and protein extraction for proteomic analysis. Gene set enrichment analysis (GSEA) was used to identify regulated functional pathways.

Results: In transcriptome analysis, IL-4, but not IL-13, upregulated genes involved in olfactory signaling (pim3, crem, creb3L1), calcium signaling (clca3b, ryr1), neuronal regeneration (ngfr, dlx3, nr4a1), and immune response (ccl8, cd163, Ly6d). In addition, IL-4, but not IL-13, downregulated genes encoding olfactory receptors (olfrs). GSEA indicated significant effects of IL-4 but not IL-13 on gene module scores for neuroimmune interactions and synaptic signaling/neuron activity. Proteomic analysis demonstrated a dominant effect of IL-4 over IL-13 on inflammatory cell recruitment to the olfactory epithelium and showed activation of neuroinflammation pathways by IL-4, but not IL-13. Finally, IL-4Rα blockade with the dupilumab surrogate restored the basal level of gene and protein expression.

Conclusion: IL-4 induces transcriptome and proteome changes suggestive of neuroinflammation and altered olfactory/calcium signaling in mouse olfactory epithelium. These findings provide mechanistic insight into the previously shown IL-4-evoked loss of smell in mice, and support the hypothesis that the therapeutic effects of dupilumab in restoring smell function in patients with CRSwNP may be mediated through inhibition of IL-4 signaling.

Conflicts of interest: Y. Hara, M.K. Jha, Y. Han, H. Mattoo, C. Zhu, A.H. Khan, and A. Hicks: Sanofi – employees, may hold stock and/or stock options in the company. S. Nash and J.M. Orengo: Regeneron

Pharmaceuticals, Inc. – employees, may hold stock and/or stock options in the company.

001366 | Genomics and metagenomics insights into the gut microbiota in cow's milk-allergic infants

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*Presenting author: E. Zubeldia-Varela

Background: Gut microbiota plays a significant role in the development of the immune system in the early stages of life. Indeed, changes in the gut microbiota have been linked to the development of food allergies (FAs), particularly one of the most prevalent food allergies in young infants: cow's milk allergy (CMA). Omics techniques allow a better understanding of the underlying mechanisms of FAs. Among them, genomics and metagenomics enable us to identify the taxonomic and functional composition of the gut microbiota. This work aims to identify bacterial taxonomy and altered metabolic pathways in infants with CMA by genomic and metagenomic analysis of faeces.

Method: 16S rRNA gene sequencing and shotgun metagenomic sequencing were performed on 26 samples from infants aged 4–6 months, thus including allergic infants (AI; n = 19) and controls (CI; n = 7), using MiSeq and NextSeq platform (Illumina, USA). Detailed epidemiological questionnaires were collected and analyzed. To identify significant differences between AI and CI groups, ANCOM-II and DESeq2 algorithms were used. The false discovery rate (FDR) approach was applied to adjust multiple hypothesis tests using the fdr.R package.

Results: Statistical analyses showed differences in the relative abundances of the *Prevotellaceae* and *Acidaminococcaceae* families (Bacteroidetes and Firmicutes phyla, respectively) between AI and CI. Besides, 15 metabolic pathways were of nominal significance between AI and CI. Four of them—glycerophospholipid, phosphatidylinositol, glycerolipids, and the phosphatidylinositol signaling system metabolisms—were increased in AI. Interestingly, glycerophospholipid metabolism was the only metabolic route with a significantly corrected p-value by FDR (< 0.05).

Conclusion: In this study, 2 bacterial families and 4 metabolic pathways related to lipid metabolism appear altered in AI. According to studies carried out by our group, AI also have altered metabolomic profiles as 2 faecal protein biomarkers compared to CI. Alterations in bacterial membranes might cause modifications in lipid metabolism at the mucosal level. Inflammation and a breakdown of the integrity of the epithelial barrier caused by FA could ensue from this affecting host immune or epithelial cells in allergic infants. These data will be integrated with the results from the other omics platforms to obtain the complete picture of the pathology.

Conflicts of interest: The authors did not specify any links of interest.

000030 | Different gut microbiota and protein expression in distinct allergic phenotypes: Data from an Asian birth cohort

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*Presenting author: A. Senavonge

Background: Allergic diseases typically originate early in life, during which interactions between the gut microbiota and host immune cells shape immune development and influence allergic phenotypes. However, whether distinct allergic phenotypes are associated with differences in gut microbiota has yet to be elucidated in a longitudinal birth cohort. Here, we sought to identify differences in gut microbial colonization and proteomic profiles in distinct allergic diseases of infants derived from a longitudinal population-based birth cohort study conducted in Thailand.

Method: Gut microbiomes isolated from the stools of infants with allergies and matched healthy controls were analyzed based on 16S amplicon sequencing and real-time PCR quantification. Proteomic

analysis was performed by liquid chromatography–tandem mass spectrometry.

Results: Participants with three atopic phenotypes [16 atopic dermatitis (AD), 5 food allergy (FA) and 5 AD+FA] and matched controls were included for study. We detected distinct gut microbial patterns and functions in participants with different allergic phenotypes as shown in figure1. Those with AD+FA phenotypes displayed the most severe dysbiosis and a dominant FA gut microbiome pattern. *Erysipelotrichaceae* colonization and high activities of these bacteria were observed in AD and AD+FA groups. Low abundances of *Bifidobacteriaceae* were detected in FA and AD+FA groups, although differences in species profiles were observed, with AD+FA participants being characterized by pathogenic *Bifidobacteriaceae* colonization. High abundances of *Bacteroidaceae* in the FA and AD+FA groups and *Enterobacteriaceae* in the FA group were also detected. Essential microbial pathways, including vitamin B_1, B_2, and K_2 pathways, were identified in AD+FA and AD participants, which are assumed to respond to allergic inflammation in human hosts as shown in table1.

Conclusion: Participants with an AD+FA phenotype exhibited the most marked changes in gut microbiome characteristics. This dysbiosis is unique and distinct from that in patients with either AD or FA.

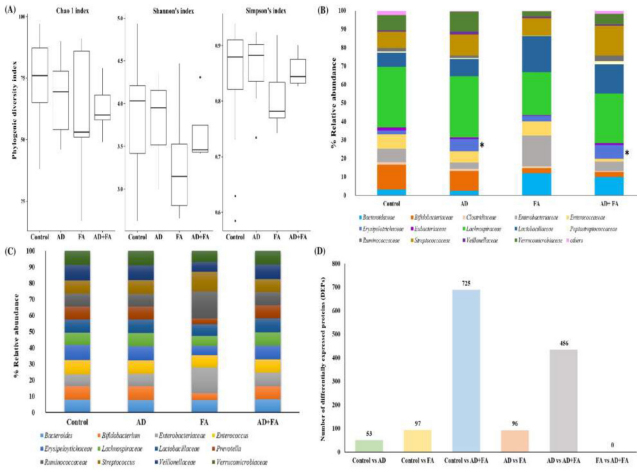

Table 4. Lists of differentially expressed proteins (DEPs) in allergic subgroup compared to controls.

Protein ID	Protein names	Families	Species	Sub-functional categories
AD+FA group				
A0A286BQV6	1-deoxy-D-xylulose-5-phosphate synthase (EC 2.2.1.7) (1-deoxyxylulose-5-phosphate synthase); thiamine (vitamin B1) synthesis pathway	*Enterobacteriaceae*	*Enterobacteriaceae bacterium JKS000234*	Metabolism of cofactors and vitamins
A0A2K9PCZ4	Riboflavin biosynthesis protein [Includes: Riboflavin kinase (EC 2.7.1.26) (Flavokinase); FMN adenylyltransferase (EC 2.7.7.2) (FAD pyrophosphorylase); riboflavin (vitamin B2) synthesis pathway	*Enterobacteriaceae*	*Citrobacter freundii complex sp. CFNIH2*	Metabolism of cofactors and vitamins
J1GBX2	Ubiquinone biosynthesis O-methyltransferase (2-polyprenyl-6-hydroxyphenol methylase); menaquinone (vitamin K2) synthesis pathway	*Enterobacteriaceae*	*Enterobacter sp. Ag1*	Metabolism of cofactors and vitamins
A0A072N8I9	Phosphoenolpyruvate carboxylase (EC 4.1.1.31); pyruvate metabolism pathway	*Bifidobacterium*	*Bifidobacterium pseudocatenulatum IPLA36007*	Carbohydrate metabolism
A0A3R9PQU3	Cellulose synthase catalytic subunit [UDP-forming] (EC 2.4.1.12); cell wall formation synthesis pathway	*Enterobacteriaceae*	*Enterobacter huaxiensis*	Carbohydrate metabolism
A0A377LPN6	6-phosphofructokinase (EC 2.7.1.11); glycolysis/gluconeogenesis pathway	*Enterobacteriaceae*	*Enterobacter cloacae*	Carbohydrate metabolism
A0A377DQK3	dTDP-D-glucose 4,6-dehydratase rmlB (EC 4.2.1.46); glycan biosynthesis and metabolism pathway	*Enterobacteriaceae*	*Escherichia coli*	Carbohydrate metabolism
U2PN91	UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase (EC 2.4.1.227) (Undecaprenyl-PP-MurNAc-pentapeptide-UDPGlcNAc GlcNAc transferase); glycan biosynthesis and metabolism pathway	*Erysipelotrichaceae*	*Faecalitalea cylindroides ATCC 27803*	Carbohydrate metabolism
A0A087D1W2	O-acetylhomoserine aminocarboxypropyltransferase (EC 2.5.1.49); cysteine and methionine metabolism pathway	*Bifidobacterium*	*Bifidobacterium scardovii*	Amino acid metabolism
U2NVC4	Aminotransferase, class I/II	*Erysipelotrichaceae*	*Faecalitalea cylindroides ATCC 27803*	Amino acid metabolism
A0A087BMC1	FabI (EC 1.1.1.100) (EC 2.3.1.41) (EC 2.3.1.86); fatty acid biosynthesis pathway	*Bifidobacterium*	*Bifidobacterium minimum*	Lipid metabolism
AD				
R6ZSA4	Demethylmenaquinone methyltransferase (EC 2.1.1.163); menaquinone (vitamin K2) synthesis pathway	*Bacteroides*	*Bacteroides sp. CAG:714*	Metabolism of cofactors and vitamins
A0A3D2W7G8	6-phospho-beta-glucosidase; glycolysis/gluconeogenesis pathway	*Erysipelotrichaceae*	*Erysipelotrichaceae bacterium*	Carbohydrate metabolism
FA				
A0A075QNH1	Pyruvate kinase (Fragment)	*Bifidobacterium*	*Bifidobacterium longum subsp. longum*	Carbohydrate metabolism

AD, atopic dermatitis, FA, food allergy

Conflicts of interest: The authors did not specify any links of interest.

000636 | Personalised genotype-based prognosing of the atopic march phenotypes in children

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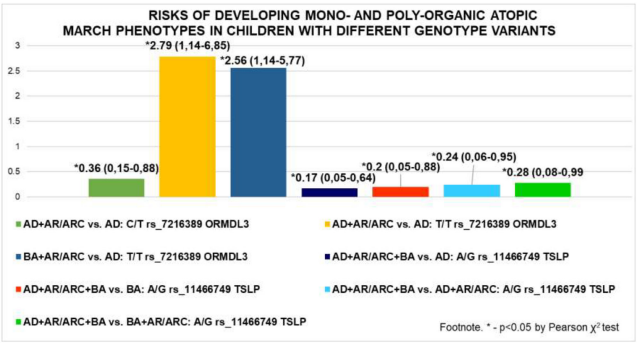
Background: Atopic march (AM) occasionally starts in childhood with the mono-organic phenotype of atopic dermatitis (AD), which could be followed by different poly-organic combinations with allergic rhinitis/rhino-conjunctivitis (AR/ARC) and bronchial asthma (BA). Single nucleotide variants (SNV) of thymic stromal lymphopoietin (*TSLP*) – rs_11466749 and orsomucoid-1-like protein 3 (*ORMDL3*) – rs_7216389 are one of the suspected ones to impact the pathogenesis of AM phenotypes. **The purpose** of the study was to detect the associations and risks of developing the poly-organic AM phenotypes within children carrying different SNV rs_11466749 *TSLP* and rs_7216389 *ORMDL3*.

Method: Children aged 3 to 18 years old were enrolled into the study: 293 suffering different AM phenotypes into the main group and 105 non-atopic – into the control group. Main group was divided into 6 phenotype clusters: mono-organic – AD, AR/ARC, BA and poly-organic -AD+AR/ARC, BA+AR/ARC, AD+AR/ARC+BA. All the patients were genotyped for SNV *TSLP* rs_11466749 and *ORMDL3* rs_7216389 by the quantitative polymerase chain reaction in real-time (qPCR). To realize the study purpose, we used Pearson correlation coefficient (r_b), odds ratio (OR) with 95% confidence interval

(95%CI), Pearson χ^2 test, Fischer exact test. Significance level was set as $p < 0.05$.

Results: Poly-organic phenotype AD+AR/ARC vs. mono-organic AD: C/T rs_7216389 *ORMDL3*: $r_b = 0.227$, OR = 0.36 (95% CI 0.15–0.88); T/T rs_7216389 *ORMDL3*: $r_b = 0.227$, OR = 2.79 (95% CI 1.14–6.85). Poly-organic phenotype BA+AR/ARC vs. mono-organic AD: T/T rs_7216389 *ORMDL3*: $r_b = 0.203$, OR = 2.56 (95% CI 1.14–5.77). Complete AM poly-organic phenotype AD+AR/ARC+BA vs. mono-organic AD: A/G rs_11466749 *TSLP* $r_b = 0.310$, OR = 0.17 (95% CI 0.05–0.64); vs. mono-organic BA: A/G rs_11466749 *TSLP* $r_b = 0.320$, OR = 0.2 (95% CI 0.05–0.88). Complete AM poly-organic phenotype AD+AR/ARC+BA vs. poly-organic AD+AR/ARC: A/G rs_11466749 *TSLP* $r_b = 0.258$, OR = 0.24 (95% CI 0.06–0.95); vs. poly-organic BA+AR/ARC: A/G rs_11466749 *TSLP* $r_b = 0.204$, OR = 0.28 (95% CI 0.08–0.99). All the results had been statistically significant.

Conclusion: Heterozygous SNV A/G rs_11466749 *TSLP* is directly protective against the complete AM poly-organic phenotype AD+AR/ARC+BA collated to AM mono-organic and other poly-organic phenotypes. Collated to the mono-organic AD phenotype, the homozygous SNV T/T rs_7216389 *ORMDL3* directly increases risk of developing the poly-organic AM phenotypes AD+AR/ARC and BA+AR/ARC, and heterozygous SNV C/T rs_7216389 *ORMDL3* is directly protective against AD+AR/ARC phenotype.



Conflicts of interest: The authors did not specify any links of interest.

Flash talks on food allergy diagnosis

000863 | Development of a murine model of shellfish allergy induced by shrimp extracts

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Background: Shellfish allergy is among the most common causes of food-induced systemic anaphylaxis. Our laboratory has previously developed a mouse model of shrimp allergy induced with tropomyosin. However, recent studies show the presence of other clinically relevant shrimp allergens beyond tropomyosin. The present study therefore aimed at developing a murine model sensitized with shrimp extracts and comparing the immunological responses with our tropomyosin-induced model.

Method: Female BALB/c mice (3–4 weeks of age) were orally sensitized and challenged with recombinant tropomyosin, raw or boiled shrimp extracts through oral gavage following our standard regimen. Systemic anaphylaxis was scored while allergen-specific IgE and IgG1 levels were measured using ELISA. mRNA expressions of Th2 cytokines in intestinal tissue were measured with RT-PCR. Continuous sections of duodenum, jejunum and ileum were assembled using Swiss roll technique for immunological and histological analyses.

Results: Based on immunoblot results, tropomyosin remained as the sole allergen despite sensitizing the animals with raw or boiled extracts. With a cut-off of 0.34 at OD450nm, the overall success rate of inducing a positive tropomyosin-specific IgE reaction was highest using boiled shrimp extract (73.7%), followed by raw extract (47.8%) and recombinant tropomyosin (34.8%). Although mice induced by boiled shrimp extract showed similar systemic allergic reaction scores and intestinal inflammatory responses (i.e. infiltration of mast cells and eosinophils) with mice sensitized by tropomyosin or raw extract, they showed a greater uplift of Th2 cytokine expression including IL-4, IL-5, IL-13 and GATA-3.

Conclusion: Tropomyosin remains the major allergen in mice sensitized with shrimp extracts. Boiled shrimp extract better sensitizes BALB/c mice, and this new model is useful for understanding the pathogenesis of shrimp allergy and for studying novel therapeutic vaccines.

Conflicts of interest: The authors did not specify any links of interest.

001582 | An advanced in vitro human mucosal immune model to predict food sensitizing allergenicity risk: A proof of concept using ovalbumin as model allergen

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*Presenting author: L. Willemsen

Background: The global demand of sustainable food sources leads to introduction of novel foods on the market, which may pose a risk of inducing allergic sensitization. Currently there are no validated *in vitro* assays mimicking the human mucosal immune system to study allergenicity risk of novel food proteins. The aim of this study was to introduce a series of sequential human epithelial and immune cell cocultures mimicking key immune events after exposure to the common food allergen ovalbumin, from intestinal epithelial cell (IEC) activation up to mast cell degranulation.

Method: This *in vitro* human mucosal food sensitizing allergenicity model combines crosstalk between IEC and monocyte-derived dendritic cells. To study the sensitizing capacities of ovalbumin in an IEC/moDC co-culture or on moDC alone, respectively the IEC cells or moDC were exposed to ovalbumin for 48h. Afterwards, the primed moDCs were collected washed and combined with naïve CD4+ T cells in the sequential coculture step. During subsequent coculture of primed CD4+ T cells with naïve B cells, IgE isotype-switching was monitored and supernatants were added to stem cell derived primary human mast cells to investigate degranulation upon IgE crosslinking. Mediator secretion and surface marker expression of immune cells were determined.

Results: Ovalbumin activated IEC and/or moDCs, resulting in downstream IgE isotype-switching upon ovalbumin exposure in presence or absence of IEC. However, only direct exposure of moDCs to ovalbumin induced Th2 polarization and a humoral B cell response allowing for anti-IgE mediated mast cell degranulation, as well as IL13 and IL4 release by the mast cells in this sequential DC-T cell-B cell-mast cell model, indicating an immunomodulatory role for IEC.

Conclusion: This *in vitro* sequential coculture model combines multiple key events involved in allergic sensitization from epithelial cell to mast cell, which can be further developed to be applied to study the allergic mechanism and sensitizing capacity of proteins.

Conflicts of interest: The authors did not specify any links of interest.

001617 | Cut-off values of allergometric tests to predict oral food challenge outcome with chicken egg in a Portuguese pediatric population

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Background: Egg allergy is common in childhood, affecting 0.5% to 2.5% of young children. Oral Food Challenges (OFC) are the gold-standard diagnostic method for food allergy. However, risk of severe allergic reactions should not be dismissed. We aim to determine cut-off values of allergometric tests that could indicate a high likelihood of a positive OFC with chicken egg.

Method: Retrospective study of children who underwent OFC in our department from Jan2013 to Dec2022. Demographic/Clinical data and last parameters before OFC: median wheal diameter (mm) with commercial extract of egg (yolk and white) and ovomucoid in SPT, fresh egg (cooked and raw) in prick-prick test(PPT) and sIgE values(kU/L) for egg (yolk and white) and ovomucoid were obtained from the clinical records. wheal size of SPT/PPT and sIgE were compared between patients with positive(G1)*vs* negative(G2) OFC. ROC curves(software IBM SPSSv21), were constructed to determine best cut-offs to predict positive OFC, with 95% confident interval and $p < 0.05$.

Results: From the total of 550 OFC, 279 (50.72%) were with chicken egg, in children with mean age of 4.9 ± 3.3 years, 185 (66.3%) were male. Of the 279 OFC with chicken egg (31 raw white; 98 cooked white; 35 raw yolk; 115 cooked yolk), 25 were positive (2;10;1;12).

For the 98 OFC with cooked white, statistically significant difference was observed between G1 vs G2 regarding median ovomucoid sIgE and wheal size of ovomucoid SPT: 2.4 (18.8) vs 0.12 (0.89), $p = 0.013$ and 5 (7.8) vs 0 (3.3), $p = 0.028$ respectively. No differences were found in median wheal size of white SPT, PPT and white sIgE levels. Only the ROC curve with discriminative capacity was the one which determined ovomucoid sIgE cut-off (>0.65 kU/L): AUC 0.73 [IC 95% 0.541–0.919], $p < 0.018$ with 70% sensibility/71.8% specificity.

For the 115 OFC with cooked yolk, statistical differences G1*vs*G2 were observed for ovomucoid sIgE and wheal size SPT: 3.79 (3.76) *vs* 0.36 (1.82), $p = 0.01$ and 8 (3) *vs* 0 (6.5), $p = 0.002$. Cut-off points determined: ovomucoid sIgE > 0.82 KU/L, AUC 0.766[IC 95% 0.65–0.89], $p = 0.013$, 87.5%sensibility/64%specificity; ovomucoid wheal size SPT > 6.5 mm, AUC 0.819, [IC 95% 0.729–0.9], $p < 0.005$ with 85.7% sensibility/75.3% especificity. For raw egg (white and yolk) series, no valid results were achieved in statistics analysis.

Conclusion: Cut-off values for ovomucoid sIgE levels and wheal size of SPT, could guide the cooked egg (white and yolk) OFC

performance in children and decrease the risk of reaction. However, its validation warrants studies on a larger scale.

Conflicts of interest: The authors did not specify any links of interest.

000576 | Identification of gibberellin-regulated protein as a new allergen in grape allergy

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*Presenting author: N. Inomata

Background: In grape allergy, nonspecific lipid transfer protein Vit v 1, which was registered as the allergen, possibly induces severe allergic reactions. In recent years, gibberellin-regulated proteins (GRPs) have been identified in other fruits, such as peaches (Pru p 7) and oranges (Cit s 7), which are related to severe allergic reactions. However, it remains unclear whether GRP allergies also include grape allergy. We investigated the allergenicity of grape GRP in grape allergy.

Method: We enrolled 22 patients diagnosed with grape allergy based on relevant clinical history, positive skin prick test (SPT) and/or challenge test. We purified grape GRP and other fruit GRPs using ion-exchange chromatography. To evaluate the allergenicity of the purified grape GRP, we performed, basophil activation tests (BATs) and SPTs with purified grape GRP and other fruit GRPs, including Pru p 7, Japanese apricot Pru m 7, cherry Pru av 7 and orange Cit s 7. Enzyme-linked immunosorbent assay (ELISA) was also performed with grape GRP. Using ImmunoCAP (Thermo Fisher Scientific), we measured specific IgE levels against grape, Japanese cedar pollen, cypress pollen, rPru p 1, rPru p 3, and rPru p 4.

Results: 13 of the 22 patients developed oropharyngeal symptoms alone, which were assigned to the oral symptom group, whereas the remaining nine patients were assigned to the non-oral symptom group. In the non-oral symptom group, six patients (66.7%) developed facial edema and two patients (22.2%) experienced anaphylactic reactions. SPTs showed positive results for grape GRP in all of the five patients in the non-oral group, whereas in the oral group there were no patients with positive SPT results for grape GRP. In addition, four of the five patients in the non-oral symptom group had positive BAT results for grape GRP, whereas all of the six patients in the oral symptom group had negative BAT results. The ELISA using nPru p 7 showed positive reactions in five of the 17 patients (29.4%). The positivity for specific IgE against grape, rPru p 1, rPru p 3 and rPru p 4 was 20%, 66.7%, 0.0% and 19.0%, respectively.

Conclusion: Grape GRP could be a novel grape allergen and may also be related to systemic reactions in grape allergy.

Conflicts of interest: The authors did not specify any links of interest.

000391 | Clinical and laboratory investigation of perilla seed allergy in Korean children

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*Presenting author: K. Jeong

Background: Perilla seeds (PS) are frequently consumed in Korea and have been recognized to cause immediate hypersensitivity reactions. However, reports on PS allergy are extremely limited worldwide and there is no commercialized test for diagnosing PS allergy. We developed a reagent for PS skin prick test (SPT) and previously reported its usefulness in diagnosing PS allergy. This study aimed to investigate clinical and laboratory profiles of PS allergy in Korean children.

Method: Clinical information and laboratory test results of children under the age of 18 with clear records of symptoms after ingestion of PS were analyzed through a retrospective medical record review from 2016 to 2022 at the Department of Pediatrics in Ajou University Hospital. Demographics, symptom pattern, anaphylaxis rate, types of PS ingested, and PS SPT results were analyzed in patients with PS allergy, and laboratory test results were compared with those who were tolerant to PS.

Results: The median ages of 38 children who had acute allergic symptoms after PS ingestion (PS-allergic) and 14 children who were tolerant to PS (PS-tolerant) were 42.5 months and 48 months, respectively. The frequency of other plant food allergies was higher in the PS-allergic group than in the PS-tolerant group. In the PS-allergic group, the rate of anaphylaxis after PS ingestion was 28.1%. The types of PS ingested were soup (36.8%), seasoning of vegetables (31.6%), PS oil (2.6%), and unknown (28.9%). Among 19 patients in PS-allergic group with a record of symptom onset time, 89.5% experienced symptoms within 10 min after PS ingestion. The median levels of total IgE in PS-allergic and PS-tolerant groups were 558 kU/L and 125.5 kU/L, respectively (p-value = 0.002). In comparison of serum sesame seed-specific IgE (SS-sIgE) levels based on the formerly suggested possibility of cross-sensitization between PS and SS, the median levels of SS-sIgE in PS-allergic and PS-tolerant groups were 5.70 kU/L and 0.09 kU/L, respectively (p-value = 0.003). The PS SPT with our own made reagent was performed in 31 out of 38 PS-allergic group and the median wheal size was 6 mm (range: 3–16 mm).

Conclusion: More than a quarter of children with PS allergy experienced anaphylaxis, and the symptom onset time was very short in most patients. In all PS-allergic children who underwent PS SPT, the wheal size was 3 mm or greater. Immunological studies for identification of PS major allergens are essential in the future.

Conflicts of interest: The authors did not specify any links of interest.

001448 | Chicken meat allergy without egg sensitization: Allergomic analysis of 5 pediatric cases

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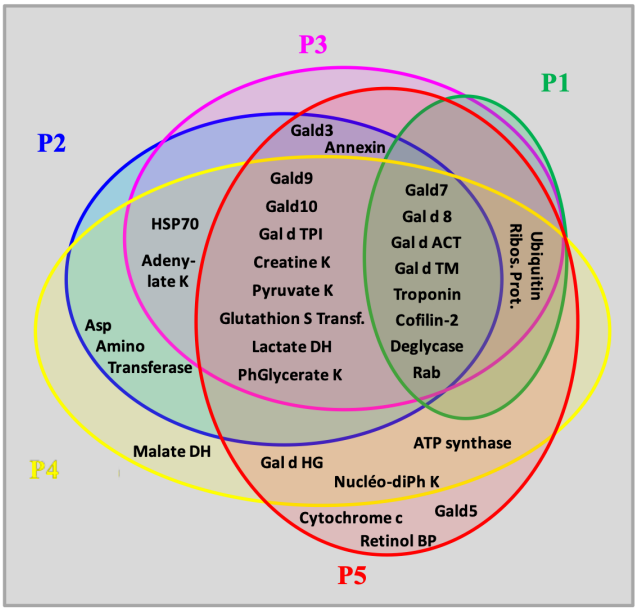
*Presenting author: T. Guiddir

Background: Although chicken meat accounts for 35% of the world's meat consumption, allergy to chicken meat remains rare. It can be the result of sensitization by ingestion of chicken meat or the extension of sensitization by eggs and/or feathers. Our objectives were to explore the allergens recognized by IgE antibodies in 5 children (P1 to P5) allergic to chicken meat without egg allergy.

Method: We performed multi-allergen chip (ALEX2©), immuno dot-line on some purified proteins, allergomic analysis (IgE immunoproteomics), i.e., 2D electrophoresis, IgE immunoblot and identification of allergens by mass spectrometry.

Results: The children had symptoms ranging from anaphylaxis to mucosal symptoms with variable skin prick tests and specific IgEs. Immunoblot analysis shows a great diversity of allergens recognized in both 1D (SDS-PAGE) and 2D analysis. P1 and P2 had the least complex and P4 and P5 the most complex protein profiles. The superposition of IgE reactivity profiles shows the existence of common reactivity ("public allergens") and reactivity more specific to the individual ("private allergens"). Two hundred and twenty-nine total proteins were identified by mass spectrometry in our cohort, including 9 proteins already described in chicken, 28 potential allergens, 12 described in other allergenic sources (other poultry, fish, crustaceans or insects) and 7 not yet described. Gal d 7, the light chain of myosin, is recognized as an allergen by all 5 children and, in addition to the allergens already described, the results show 10 "new" proteins as potential allergens.

Conclusion: Allergy to chicken meat involves more than the 13 allergens already described in the literature. The observed IgE reactivity profiles are not absolutely associated with clinical symptoms but the characterization of molecular allergens allows a better understanding of potential cross-reactivities with other allergenic sources.



Conflicts of interest: The authors did not specify any links of interest.

001607 | Cut-off values of allergometric tests to predict oral food challenge outcome in cow´s milk Portuguese allergic children

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Background: Cow's milk allergy is common in childhood, affecting about 1.9% to 3% of young children. Oral Food Challenges (OFC) are the gold-standard diagnostic method for food allergy, however, the risk of severe allergic reactions should not be dismissed. Wheal size in skin prick tests (SPT) and serum-specific IgE (sIgE) levels have been studied as predictors of OFC outcome. We aim to determine the diagnostic values of allergometric tests to predict the safety and outcome of OFC with cow'milk.

Method: Retrospective study of children who underwent OFC with cow´s milk in our department, from Jan 2013 to Dec 2022. Demographic/Clinical data and last parameters performed before OFC: mean wheal diameter (mm) with commercial extract of milk and casein in SPT and with fresh cow´s milk in prick-prick test (PPT) and sIgE values (KU/L) for milk and casein were obtained from the clinical records. Wheal size in SPT/PPT and sIgE were compared between patients with positive (G1) *vs* negative (G2) OFC. ROC curves (software IBM SPSS version 21), were constructed to determine the best cut-offs to predict positive OFC, with 95% confident interval and $p < 0.05$.

Results: From the total of 550 OFC, 138(25%) were with cow´s milk, in children with mean age of 3.9 ±3.2 years, 92(66.7%) were male. OFC with cow's milk was positive in 14(10.1%) patients. Statistically significant differences were obtained between G1vsG2, regarding the median (IQR) casein sIgE levels, milk sIgE levels, wheal size of SPT with casein and milk: 1.3(3.5) vs 0.2 (0.5) kU/L, p = 0.002; 2.4 (8.54) vs 0.37(0.9) kU/L, p = 0.001; 4.5(7.3) *vs* 0(4) mm, p < 0.001; 4(4) *vs* 0 (3) mm, p = 0.048. No significant difference was observed in the median wheal size of PPT with fresh milk between the groups: 4.5 (7.3) vs 0 (5.8) mm, p = 0.06.

Cut-off points were obtained for: casein sIgE >0.24 KU/L, ROC curve (AUC 0.749, [IC 95% 0.71–0.94], p = 0.003) with 84.6% sensibility and 57.3% specificity; milk sIgE >0.65 KU/L, ROC curve (AUC 0.823 [IC 95% 0.71–0.94], p < 0.001) with 83.3% sensibility and 69.1% specificity; wheal size of SPT with casein >3.5mm, ROC curve (AUC 0.789 [IC 95% 0.66–0.92], p = 0.003) with 60% sensibility and 74.3% specificity. The ROC curve obtained for median wheal size of SPT with milk had no discriminative capacity (AUC <0.7).

Conclusion: Determine and use cut-off values in allergometric tests for each allergic population could guide the milk OFC performance in children and decrease the risk of reaction. However, its validation warrants studies on a larger scale.

Conflicts of interest: The authors did not specify any links of interest.

000279 | Retrospective study evaluating molecular sensitization profile in patients with lipid transfer protein syndrome (LTP) in Murcia, Spain

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*Presenting author: S. San Roman Sirvent

Background: We conducted a preliminary, retrospective data analysis to evaluate the molecular sensitization profile in patients with LTP syndrome. We aimed to characterize and describe whether patients with anaphylaxis displayed significant differences in nsLTP sensitization detected by microarray, compared with patients without systemic symptoms. We also investigated the association between microarray and skin prick test sensitization.

Method: Seventy-five patients with LTP syndrome were retrospectively recruited and divided into two groups: 50 patients with anaphylaxis and 25 patients with local symptoms (oral allergy syndrome and/or urticaria). We performed skin tests with tree pollen extracts (Artemisia vulgaris, Olea europaea, Platanus acerifolia) and plant-food extracts (peach, walnut, peanut, hazelnut and wheat) as well as component-based allergy diagnosis by microarray.

Results: Pru p 3 was the most frequent sensitizer in both groups of patients, followed by Jug r 3. Patients with anaphylaxis showed a greater percentage of sensitization to all nsLTPs except for Jur g 3, which was slightly higher in the non-anaphylactic group. In addition, monosensitization to Jug r 3 was only observed in patients without systemic symptoms (8%). The risk of anaphylaxis was significantly higher in patients sensitized to Pla a 3 (OR=3.57, p-value = 0.018), followed by Tri a 14 (OR = 4.03, p-value = 0.084). Several patients who associated respiratory symptoms (rhinitis and/or asthma) were sensitized to Pla a 3, while asthmatic patients showed greater percentage of sensitization to Par j 2. Finally, there was a significant association between microarray and skin prick test results for all allergens, except peach and olive pollen.

Conclusion: Based on our results, we can conclude that Pru p 3 is the major allergen in all patients, followed by Jug r 3. Furthermore, patients with local symptoms are characterized by Jug r 3 monosensitization and show a lower number of nsLTP sensitization in microarray. Pla a 3 and Tri a 14 are the most distinctive allergens in patients with anaphylaxis, and Par j 2 should be considered as a possible risk factor for asthma in patients with LTP Syndrome, however further studies are required. Finally, skin prick tests seem useful except for peach and wheat, which are poorly associated with microarray results.

Conflicts of interest: The authors did not specify any links of interest.

000467 | Identification of 2s-albumins as marker allergens of sunflower seed allergy

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*Presenting author: S. Hazebrouck

Background: Allergy to sunflower seed (SFS) has been rarely studied but increasing consumption of this source of protein, as an alternative to animal protein, may lead to more frequent cases of anaphylaxis. To date only Hel a 3, a non-specific lipid transfer protein (nsLTP), is recognized as a food allergen. Among the eleven seed storage 2S-albumins (SESA) detected in SFS, SFA-8 is currently considered as a rather weak allergen but allergenicity of the other SESA still needs to be investigated.

Method: The IgE-binding to the most abundant SESA, i.e. SESA2-1, SESA20-2 and SFA-8, and nsLTP was analyzed by using two different formats of immunoassay, with sera from 17 patients allergic to SFS and from 13 patients tolerant to SFS but allergic to fruit and/or nuts. The IgE cross-reactivity between nsLTP from SFS (Hel a 3), peach (Pru p 3) and peanut (Ara h 9) and between SESA was evaluated by competitive inhibition of IgE-binding. Elicitation potencies of the SESA were also compared in a degranulation assay using RBLSX-38 cells.

Results: We evidenced two different profiles of sensitization to SFS protein. One corresponded to patients with LTP syndrome. A strong IgE cross-reactivity was then observed between Hel a 3, Pru p 3 and Ara h 9. However, Pru p 3 did not appear as a common primary sensitizer, thus suggesting that exposures to different food or pollen could induce IgE sensitization to Hel a 3. For the second profile, IgE

sensitization to at least one SESA was detected in the absence of IgE sensitization to Hel a 3. A strong IgE cross-reactivity was also evidenced between SFA-8, SESA2-1 or SESA20-2 but only the two latter 2S-albumins appeared as potential markers for a specific sensitization to SFS and for more severe allergic symptoms.

Conclusion: Our work revealed that SESA2-1 and SESA20-2 displayed higher allergenic potencies than SFA-8. Sensitization to SESA2-1 and SESA20-2 also appeared to be more specific for moderate and severe symptomatic SFS allergy than sensitization to SFA-8 or Hel a 3. These results should be confirmed in larger studies.

Conflicts of interest: The authors did not specify any links of interest.

001270 | Outcome of sesame oral food challenges – a single center experience

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Background: Sesame allergy has been recognized as a growing food allergy of global proportions. In Israel sesame was found to be the third most common allergen, preceded only by milk and eggs and second only to milk as a cause of anaphylaxis. Tolerance to sesame develops in only 20%–30% of patients. Clinical characteristics and SPT are the main tools we use to help us with deciding on performing OFC. However, the diagnostic accuracy of these tools has been suboptimal. Our objective was to describe sesame OFC outcomes and assess the predictive value of clinical history and SPT testing.

Method: Retrospective chart review of all sesame OFCs performed at the pediatric allergy clinic at the Wolfson Medical Center between 2016 and 2020.

Results: 83 patients, (66% male) underwent sesame OFC at an average age of 4.8 years (range 0.7–16.9 years). 53 patients (64%) had a negative sesame OFC and 15 patients were intermediate (18%). 15 patients (18%) had a positive OFC with a median eliciting dose of 108 mg of sesame protein. One patient required adrenaline. Among our patients 47 (57.1%) had atopic dermatitis, 35 (41.7%) had asthma and 16 (19%) had allergic rhinitis. 40 patients (48.2%) had allergy to other foods (mainly peanuts and tree nuts). Average SPT was 5mm (range 0–15 mm). Positive sesame OFC was significantly associated with a history of at least one atopic disease (asthma, atopic dermatitis and/or allergic rhinitis) ($p = 0.0002$). Age, SPT, asthma, atopic dermatitis, allergic rhinitis, allergy to other foods, history of a previous allergic reaction to sesame and age at diagnosis were not significantly different between positive and negative sesame OFC.

Conclusion: In our patients we observed a higher rate of achieving tolerance to sesame than previously reported. SPT with a commercial extract was not predictive of the OFC outcome. A medical history of atopy was the only parameter associated with positive sesame OFC and may be used as a risk factor when considering performing an OFC.

Conflicts of interest: The authors did not specify any links of interest.

001614 | Using big data to study fish allergy profile in our area

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Background: Fish allergy is one of the most common food allergies, particularly in children. It is generally IgE-mediated and tends to elicit severe reactions. Polysensitization and clinical cross-reactivity among various fish species is frequent, however certain species can be tolerated.

The aim of this study was to describe epidemiological features, comorbidities, sensitization, and tolerance profile of children with fish allergy in our area using big data analysis.

Method: We conducted a retrospective descriptive study (2018–2022) in the Allergy Unit of Infanta Leonor University Hospital (Madrid, Spain). Data were collected from electronic clinical history using Ehreader technologie of Savanna programme, tool used in our hospital.

Different variables were included: age, sex, family history of atopy, personal history of atopic dermatitis, allergic rhinitis, asthma, other food allergies. Other data like first fish elicitor of the allergic reaction, skin prick test, specific IgE and oral challenge to different fish species were studied.

Results: 56 patients with fish allergy were included. Medium age at onset of fish allergy reaction was 2 years (range: 7 months-15 years old) and 54% were male.

Regarding comorbidities, 86% were atopic: 63% atopic dermatitis, 46% allergic rhinitis, 27% asthma and 68% had other food allergies (50% nuts, 36% fruits, 34% seafood, 34% egg, 14% legumes and 14% milk).

The most frequent symptom was urticaria (48%) followed by oral allergy syndrome (16%) and angioedema (13%). Anaphylaxis appeared in 5.4% of our sample. Hake was the culprit allergen in 46% of the cases. 82% of our patients were polysensitized to various fish species.

Describing serum specific IgE, 88% were sensitized to codfish (mean 13kU/L), 88% to whiff (mean 3kU/L) and 79% to hake (mean 3 kU/L). After oral challenge, 75% tolerated at least another fish species: tuna (57%), swordfish (49%) and salmon (28%). Only 7% of our patients outgrew their fish allergy.

Conclusion: Big data technology is a useful tool for analysing allergic patterns. In our study, fish allergic profile tends to be a pre-schooled subject with atopic dermatitis, polysensitized to various fish species with the minority outgrowing their fish allergy.

Conflicts of interest: The authors did not specify any links of interest.

000222 | White meat fish allergy in Korean children: A single hospital based retrospective study

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*Presenting author: S. Youm

Background: Fish allergy is relatively rare in children and there are few studies conducted on fish allergy worldwide. In this study, we aim to investigate the clinical characteristics and laboratory findings of white meat fish allergy in Korean children.

Method: Sixty-five children with a history of ingesting white meat fish who underwent serum specific immunoglobulin E to cod (cod-sIgE) assay (ImmunoCAP; Thermo Fisher, Uppsala, Sweden) at Ajou University Hospital were enrolled through a retrospective medical record review from January 2019 to July 2022. The demographic characteristics, clinical symptoms, causative fish, and serological test results were investigated.

Results: Thirty-six subjects (55.4%) presented with clinical white meat fish allergy (WMF-allergic), and 29 subjects were without allergic reaction after ingestion of white meat fish (WMF-tolerant). The median age of first symptom in WMF-allergic group was 15.5 months. The major causative white meat fish in the WMF-allergic patients were cod (41.7%), yellow croaker (33.3%), hairtail (30.6%), and brown sole (27.8%). Nine out of 36 WMF-allergic children (25%) had anaphylaxis. The median level of cod-sIgE was 4.7 kU/L (range, 0.04–68.7 kU/L) in the WMF-allergic group, and this value was significantly higher ($p < 0.0001$) than that of the WMF-tolerant group (0.04 kU/L; range, 0.04–7.29 kU/L), with an optimal cutoff level of 1.81 kU/L (sensitivity 72.22%; specificity 89.66%). The cod-sIgE level with 100% specificity was 7.29 kU/L. When classified by the symptoms regarding cod (not all types of white meat fish), the median level of cod-sIgE of 15 patients with cod allergy was 4.78 kU/L (range, 0.04–68.7 kU/L), and this value was significantly higher ($p = 0.0001$) than that of the cod tolerant children (0.04 kU/L; range, 0.04–11.2 kU/L), with an optimal cutoff level of 0.41 kU/L (sensitivity 73.33%; specificity 100%).

Conclusion: In this study, we proposed that white meat fish allergy can develop in young children. Anaphylaxis was observed in 25% among WMF-allergic children. Cod-sIgE has useful value in diagnosing not only cod allergy but also in other white meat fish allergies in children.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on asthma treatment

000854 | Real-world outcomes of patients with severe asthma treated with mepolizumab by baseline inhaled corticosteroid dose: Post hoc analysis of realiti-a at 2 years

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*Presenting author: C. Caruso

Background: In line with the Global Initiative for Asthma 2022 guidelines, patients with severe asthma undergo a stepwise treatment progression from medium (>250–500 µg/day fluticasone propionate [FP] equivalent) to high-dose (>500 µg/day) maintenance inhaled corticosteroids (mICS) before consideration of biologic therapies, such as mepolizumab, for disease control. Real-world mepolizumab treatment reduces clinically significant asthma exacerbations (CSEs) and oral corticosteroid (OCS) use, while improving symptom control in patients with severe eosinophilic asthma (SEA). We assessed the real-world impact of mepolizumab in patients with SEA, using data from REALITI-A at 2 years, stratified by mICS dose.

Method: REALITI-A (GSK ID: 204710) was a 2-year, prospective observational cohort study enrolling adult patients with asthma, newly prescribed mepolizumab 100 mg subcutaneously (index), at the physician's discretion. Data were collected for 12 months pre- and 24 months following mepolizumab initiation. This post hoc analysis assessed outcomes in patients stratified by baseline mICS dose (>250–≤500, >500; µg/day, FP equivalent). Outcomes included the rate of CSEs (requiring systemic corticosteroids and/or emergency department visit/hospitalisation) pre- and following mepolizumab, change from baseline (28 days before index) in daily maintenance OCS (mOCS) dose to Week 101–104, and change from baseline (90 days before index) in Asthma Control Questionnaire (ACQ)-5 score at Month 24.

Results: For the 822 patients treated, baseline mICS dose data was available for 774 (**Table**). Versus pre-mepolizumab, the rate of CSEs following mepolizumab reduced by 80% and 73% in the medium and high mICS dose subgroups, respectively. For patients with baseline mOCS use, median mOCS dose also reduced from baseline at Week 101–104 by 85% and 100% for the medium and high mICS dose subgroups, respectively, with 45% and 58% of patients discontinuing mOCS. For the high mICS dose subgroup (medium mICS subgroup non-estimable), least squares mean ACQ-5 score improved from baseline by 1.5 points at Month 24.

Conclusion: This post hoc analysis of data from the REALITI-A study at 2 years highlight that following mepolizumab treatment patients with SEA had reduced CSEs and mOCS dose, paralleled by improved symptom control. These findings were irrespective of baseline mICS

dose and highlight that patients with SEA uncontrolled on medium mICS doses benefit from mepolizumab treatment.

Table. REALITI-A outcomes at 2 years, stratified by medium and high baseline mICS dose compared with the treated population

Outcomes	Treated population (n=822)	Baseline mICS dose* (µg/day) (n=774)†	
		Medium (>250–≤500) (n=104)	High (>500) (n=667)
CSEs, events/year			
Pre-mepolizumab	n=821 4.25	n=104 3.39	n=666 4.38
Following mepolizumab	n=820 1.11	n=104 0.67	n=665 1.19
Rate ratio (95% CI) (following vs pre-mepolizumab)	0.26 (0.24, 0.29)	0.20 (0.14, 0.28)	0.27 (0.25, 0.30)
mOCS dose,‡ mg/day median (IQR)			
Baseline§	n=297 10.0 (5.0, 14.7)	n=38 7.8 (5.0, 12.5)	n=249 10.0 (5.0, 15.0)
Week 101–104	n=168 0.0 (0.0, 5.0)	n=20 1.2 (0.0, 3.8)	n=144 0.0 (0.0, 5.0)
Patients with a 100% reduction from baseline at Week 101–104, n (%)	n=168 95 (57)	n=20 9 (45)	n=144 84 (58)
ACQ-5 score, LS mean			
Baseline‖	n=781 2.9 (2.8, 3.0)	NE¶	n=635 2.9 (2.8, 3.0)
Month 24	n=194 1.3 (1.2, 1.5)	NE¶	n=163 1.4 (1.2, 1.5)
Change from baseline at Month 24	-1.5 (1.7, -1.4)	NE¶	-1.5 (-1.7, -1.4)

*Fluticasone propionate equivalent dose; †3 subjects with baseline mICS low dose were excluded from this analysis; ‡prednisolone equivalent dose; §in the 28 days before mepolizumab initiation; ‖in the 90 days before mepolizumab initiation; ¶value not estimable due to paired sample numbers being too low.

ACQ-5, Asthma Control Questionnaire-5; CI, confidence interval; CSE, clinically significant asthma exacerbation; IQR, interquartile range; LS, least squares; mICS, maintenance inhaled corticosteroid; mOCS, maintenance oral corticosteroid; NE, not estimable.

Conflicts of interest: RA-C, RGP and PH are employees of GSK and own stocks/shares in GSK. TW received grants and personal fees for lectures and advisory boards from AstraZeneca, personal fees for lectures and advisory boards from Berlin-Chemie, Novartis and Sanofi, personal fees for advisory boards from GSK. CP has received fees for advisory boards, speaker meetings and research grants from GSK, AstraZeneca, Chiesi, Novartis, Teva and ALK-Abelló. CC has received research grants and lecture fees from GSK and AstraZeneca. AS and MP have received lecturing fees and participated in clinical trials with AstraZeneca and GSK, and participated in clinical trials with Chiesi, Oncimmune, Novartis and Teva.

001533 | Towards standardisation of clinical outcomes used in allergen immunotherapy in allergic asthma

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*Presenting author: J. Kappen

Background: For the co-authors:

Zuzana Diamant, Ioana Agache, Matteo Bonini, Jean Bousquet, G. Walter Canonica, Stephen R. Durham, George V. Guibas, Eckard Hamelmann, Marek Jutel, Nikolaos G. Papadopoulos, Graham Roberts, Mohamed H. Shamji, Petra Zieglmayer, Roy Gerth van Wijk

In allergic asthma patients, one of the more common phenotypes might benefit from allergen immunotherapy (AIT) as add-on intervention to pharmacological treatment. AIT is a treatment with disease-modifying modalities, the evidence for efficacy is based on controlled clinical trials following standardized endpoint measures. However, so far there is a lack of a consensus for asthma endpoints in AIT trials. The aim of a Task Force (TF) of the European Academy of Allergy and Clinical Immunology (EAACI) is evaluating several outcome measures for AIT in allergic asthma.

Method: The following domains of outcome measures in asthmatic patients have been evaluated: (i) Exacerbation rate, (ii) Lung function, (iii) ICS withdrawal, (iv) Symptoms and rescue medication use, (v) Questionnaires (PROMS), (vi) bronchial/nasal provocation, (vii) Allergen Exposure Chambers (AEC), (viii) Biomarkers.

Results: This EAACI-TF highlighted important aspects of current asthma measures by critically evaluating their applicability for controlled trials of AIT.

Conclusion: Exacerbation rate can be used as a reliable objective primary outcome, although there is limited evidence due to different definitions of exacerbation. Furthermore, the endpoints for allergic asthma and AIT are often more subtle. It is therefore advised that symptom scores and medication use (ICS and reliever medication reduction) are used as clinical outcomes in AIT in asthma patients. All are clinical applicable and easy to use, there is however the urgent need for standardization for use in clinical trials. ACQ5/ AQLQ and CARAT are well established PROMs questionnaires, however, validation addressing asthma control in relation to AIT is an unmet need. After ICS withdrawal the time to first exacerbation can be captured as primary outcome measure.

FeNO and eosinophil levels (evaluated in clinical context) have the potential to become surrogate biomarkers of clinical response. Additional studies are needed to confirm and to interpret their association with the clinical response to immunotherapy.

Finally, future systemic RWE data is needed to analyze the suggested outcome measures, novel eHealth tools can support these evaluations.

Conflicts of interest: The authors did not specify any links of interest.

000024 | Airway epithelial antiviral immunity is enhanced by allergen immunotherapy in allergic asthma

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*Presenting author: C. Porsbjerg

Background: Allergic asthma is linked with impaired bronchial epithelial secretion of antiviral interferons (IFNs) which may be causally

linked with the increased risk of viral exacerbations. We have previously shown that allergen immunotherapy (AIT) effectively reduces asthma exacerbations and prevents respiratory infections requiring antibiotics; however, whether AIT alters antiviral immunity is still unknown. Hence the aim of this study was to investigate the effect of house dust mite sublingual immunotherapy (HDM-SLIT) on the bronchial epithelial antiviral and inflammatory responses in patients with allergic asthma.

Method: In this double blind randomized controlled trial (VITAL), adult patients with HDM allergic asthma received HDM-SLIT 12-SQ or placebo for 24-weeks. Bronchoscopy was performed at baseline and at week-24 which included sampling for human bronchial epithelial cells (HBECs). HBECs were cultured at baseline and at week-24 and stimulated with the viral mimic poly(I:C). mRNA expression was quantified by RT-qPCR and protein levels were measured by multiplex ELISA.

Results: Thirty-nine patients were randomized to HDM-SLIT (n = 20) or placebo (n = 19). HDM-SLIT resulted in increased poly(I:C)-induced expression of IFN-β, both at gene (p = .009) and protein (p = 0.02) level. IFN-λ gene expression was also increased (p = 0.03), whereas IL-33 tended to be decreased (p = 0.09). Pro-inflammatory cytokines IL-6 (p = .009) and TNF-α (p = 0.08) increased compared with baseline in HDM-SLIT group. There was no significant change in TSLP, IL-4, IL-13, and IL-10.

Conclusion: HDM-SLIT improves bronchial epithelial antiviral resistance to viral infection while altering the inflammatory response. These results potentially explain the efficacy of HDM-SLIT reducing exacerbations in allergic asthma.

Conflicts of interest: Dr. Woehlk has previously received speakers honoraria from ALK Abelló and is currently in a temporary research position with them. The study was performed as a phd-study without any interference from the company.

000461 | Evaluation of disease control after SARS-CoV-2 infection and/or vaccination in patients with NSAID-exacerbated respiratory disease

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Background: There is insufficient data on changes in disease control following SARS-CoV-2 infection and/or vaccination in patients with non-steroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD). This study aimed to investigate the history of COVID-19 in patients with N-ERD, determine whether they experienced exacerbations of asthma or rhinitis following COVID-19 and evaluate their post-vaccination asthma and rhinitis control data.

Method: The demographic characteristics of patients with N-ERD, and whether they have had symptoms of asthma, changes in nasal symptom scores (SNOT-22), asthma control test (ACT) within one month after SARS-CoV-2 vaccination or infection were recorded. The prevalence of COVID-19 in N-ERD patients and healthy controls was estimated.

Results: A total of 103 N-ERD patients and 100 healthy controls were included in the study. Thirty-seven (35.9%) of the patients with N-ERD and 65 (65%) of the controls had a history of COVID-19. There was no significant difference in changes in the ACT and SNOT-22 scores after SARS-CoV-2 vaccination (p = 0.999). After first COVID-19, the patients with N-ERD had significant decrease in their ACT scores (p = 0.017; r=0.39). Level of asthma control was not impaired after infection (p < 0.001) (Figure 1).

Conclusion: The history of COVID-19 was less frequent in the N-ERD group. There was no deterioration in asthma and rhinitis controls after SARS-CoV-2 vaccination. While a significant decrease was observed in the ACT scores after COVID-19, there was no deterioration in the level of asthma control.

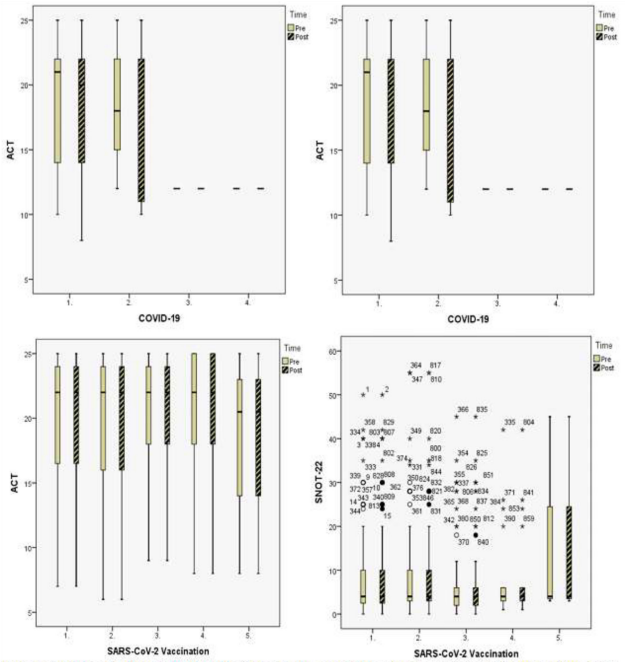

Figure 1: Changes in asthma control test (ACT) and sino-nasal obstruction test (SNOT-22) scores before, after severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccination and coronavirus disease 2019 (COVID-19)

Conflicts of interest: The authors did not specify any links of interest.

001646 | **TMT-based quantitative proteomic analysis reveals downregulation of ITGAL and Syk by the effects of cycloastragenol in ova-induced asthmatic mice**

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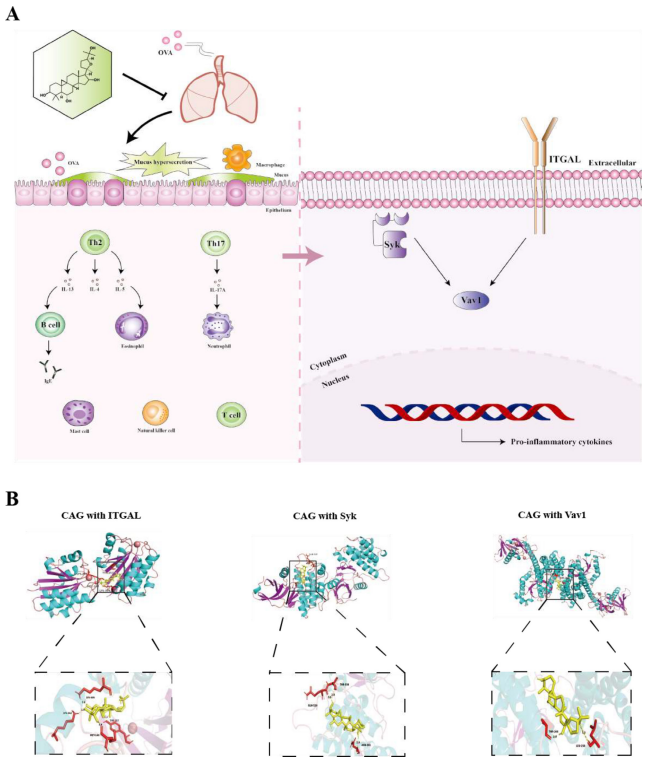
*Presenting author: X. Zhu

Background: Cycloastragenol (CAG) has been reported to alleviate airway inflammation in ovalbumin- (OVA-) induced asthmatic mice. However, its specific mechanisms remain unclear. This study is aimed at investigating the effects of CAG on asthma, comparing its efficacy with dexamethasone (DEX), and elucidating the mechanism of CAG's regulation.

Method: The asthma mouse model was induced by OVA. CAG at the optimal dose of 125 mg/kg was given every day from day 0 for 20-day prevention or from day 14 for a 7-day treatment. We observed the preventive and therapeutic effects of CAG in asthmatic mice by evaluating the airway inflammation, AHR, and mucus secretion. Lung proteins were used for TMT-based quantitative proteomic analysis to enunciate its regulatory mechanisms.

Results: The early administration of 125 mg/kg CAG before asthma happened prevented asthmatic mice from AHR, airway inflammation, and mucus hypersecretion, returning to nearly the original baseline. Alternatively, the administration of CAG during asthma also had the same therapeutic effects as DEX. The proteomic analysis revealed that the therapeutical effects of CAG were associated with 248 differentially expressed proteins and 3 enriched KEGG pathways. We then focused on 3 differentially expressed proteins (ITGAL, Syk, and Vav1) and demonstrated that CAG treatment downregulated ITGAL, Syk, and Vav1 by quantitative real-time PCR, western blot analysis, and immunohistochemical staining.

Conclusion: These findings suggest that CAG exerts preventive and protective effects on asthma by inhibiting ITGAL, Syk, and the downstream target Vav1.



Conflicts of interest: The authors did not specify any links of interest.

001595 | **Role of sex hormones in B2-receptor-mediated relaxation in bronchial tissue**

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*Presenting author: I. Cerqua

Background: Bronchial hyperresponsiveness is the main risk factor for the development and progression of asthma. In this context, β_2 agonists represent an important therapeutic weapon. However, even if inhaled β_2-agonists are among the most prescribed drugs for asthma, their efficacy is quite variable. Clinical evidence shows an important degree of heterogeneity in the therapeutic response to β_2-agonists. Recent literature recognized sex differences as a significant non-modifiable risk factor in asthma pathogenesis and therapy. Here we have investigated the role of sex hormones in the modulation of β_2-mediated bronchial relaxation.

Method: β2-mediated bronchial relaxation has been evaluated in male and female mice of different strains (BALB/c; C57BL/6; CD1). Molecular and functional studies have been performed. In a different set of experiments bronchi harvested from estradiol-treated male mice and tamoxifen-treated female mice have been used.

Results: Functional studies show that sex differences in β_2-mediated broncho-relaxation are evident in all strains used. However, this sex difference becomes more significant in BALB/c mice. The increased relaxing response to salbutamol observed in male mice is not associated with a higher expression of β_2-receptors in bronchial tissue.

Accordingly, the functional inhibition of adenylate cyclase equally affected salbutamol-induced relaxation in both sexes. Also, the sensibility to cyclic-AMP of bronchi harvested from both sexes was the same. However, western blot analysis showed an increased expression of phosphodiesterase 4a (PDE4a) in bronchi harvested from females, and the functional inhibition of this enzyme significantly increased salbutamol-induced relaxation only in females. Further, estradiol treatment reduced the β_2-mediated broncho-relaxation in males and this effect was restored by the inhibition of PDE4a. In accordance with functional data, western blot confirmed the upregulation of PDE4a in estradiol-treated mice. Conversely, the modulation of estradiol by treating females with tamoxifen enhanced the β_2-mediated broncho-relaxation.

Conclusion: The results confirm the key role of sex hormones in the β_2-receptors mediated relaxation resulting in a different β_2-agonists sensibility between sexes. Collectively, investigating the specific effects of sex on β2-receptors mediated relaxation may provide support for the management of people with airway diseases such as asthma via personalized genotype- and sex-specific therapies.

Conflicts of interest: The authors did not specify any links of interest.

000373 | The comparison study on accuracy of the novel digital peak expiratory flow device compared to conventional peak flow meters

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*Presenting author: S. Chaiparnich

Background: Digital Peak Expiratory Flow Device (D-PEF Device) was developed to measure and record Peak Expiratory Flow (PEF) values for asthma monitoring. It was designed to function independently but it also came with a multi-functional mobile application that was designed for personalized monitoring and data analysis.

The study aims to primarily compare the accuracy of D-PEF Device to the gold standard spirometry as well as to an available peak expiratory flow measuring device, namely, Mini-Wright peak flow meter. A cross-sectional comparison study was conducted comparing D-PEF Device with the spirometry among 55 healthy volunteers. A similar comparison study between the D-PEF Device and Mini-Wright peak flow meter was conducted among 28 healthy volunteers.

Method: Peak expiratory flow (PEF) value was collected from the subjects by means of D-PEF Device, the spirometry and by Mini-Wright peak flow meter. Paired t-test, Pearson Correlation Coefficient, and Bland-Altman plot were used for the statistical analysis for both comparison studies.

Results: D-PEF Device and the Spirometry

There is no significant difference between the PEF values collected by D-PEF Device and the spirometry, $t(54)$, $p > 0.05$. The Pearson Correlation R reveals strong correlation, $r[55] = 0.84$, $p < 0.001$. The Bland-Altman Plot shows that 94.54% of the data collected are within the limit of agreement (LOA) as shown in Figure 1.

D-PEF Device and Mini-Wright Peak Flow Meter

There was no significant difference in the PEF values measured by D-PEF Device and Mini-Wright peak flow meter; $t(27)$, $p > 0.05$. The Pearson Correlation R shows that PEF values collected by D-PEF and Mini-Wright peak flow meter were strongly correlated, $r[28] = 0.96$, $p < 0.001$. The Bland-Altman plot shows that 89.29% of the mean differences between the two devices lie within the LOA as shown in Figure 2.

Conclusion: It is evidential that the accuracy of the novel D-PEF Device are in agreement with the spirometry and with Mini-Wright peak flow meter. The integration of D-PEF Device may potentially lead to new monitoring strategies that healthcare providers can use to improve the overall management.

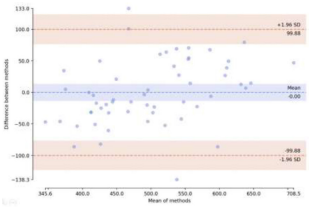

Figure 1. Bland-Altman Plot of D-PEF Device and the Spirometry

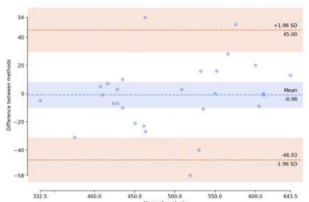

Figure 2. Bland-Altman Plot of D-PEF Device and Mini-Wright Peak Flow Meter

Conflicts of interest: The authors did not specify any links of interest.

000919 | Impact of age of asthma onset on the long-term efficacy of Dupilumab in patients with type 2 inflammation: Liberty asthma traverse study

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*Presenting author: N. Pandit-Abid

Background: Age of asthma onset is a clinical phenotype, showcasing the heterogeneity of asthma presentation, and underlying complexity of the disease pathophysiology. Dupilumab, a human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, key and central drivers of type 2 inflammation. In the

phase 3 LIBERTY ASTHMA QUEST study (NCT02414854), add-on dupilumab significantly reduced severe asthma exacerbations and improved lung function for up to 52 weeks versus matched placebo in patients with moderate-to-severe asthma. LIBERTY ASTHMA TRAVERSE is an open-label extension study (NCT02134028) evaluating the long-term safety and efficacy of dupilumab in patients from QUEST. Safety of dupilumab in TRAVERSE was consistent with the previous safety profile. This post hoc analysis aimed to evaluate the efficacy of dupilumab according to age of asthma onset in patients with type 2 inflammation (blood eosinophils ≥ 150/μL or fractional exhaled nitric oxide ≥ 25 ppb) from QUEST who enrolled in TRAVERSE.

Method: Patients were stratified by age of asthma onset (< 18 years, 18–40 years, or ≥ 40 years). Endpoints: annualized severe exacerbation rate (AER) during QUEST (Weeks 0–52) and TRAVERSE (Weeks 0–48 and Weeks 48–96) and change from parent study baseline (PSBL) in pre-bronchodilator FEV_1 over QUEST and TRAVERSE.

Results: 1279 patients were included in these analyses. In patients treated with dupilumab through QUEST and study extension TRAVERSE, AER were reduced during QUEST and continued to decline during TRAVERSE, independent of age of asthma onset **Table**). Furthermore, significant improvements in lung function from PSBL during QUEST were maintained in TRAVERSE. In patients who received placebo during QUEST, dupilumab demonstrated a significant reduction in AER and lung function improvement, which were maintained to Week 96 in all asthma age-onset subgroups (**Table**).

Conclusion: Dupilumab demonstrated sustained reductions in AER and improvement in lung function in all moderate to severe asthma age-onset groups up to 148 weeks.

Table. Summary of efficacy outcomes in patients with type 2 inflammation rolled over from QUEST into TRAVERSE by age of asthma onset.

	Age of onset < 18 years		Age of onset 18-40 years		Age of onset ≥ 40 years	
	PBO/DPL (n = 155)	DPL/DPL (n = 310)	PBO/DPL (n = 151)	DPL/DPL (n = 299)	PBO/DPL (n = 131)	DPL/DPL (n = 233)
Unadjusted AER						
Parent study baseline	1.97	1.87	2.40	2.29	2.4	2.11
During QUEST	0.738	0.502	1.294	0.485	1.335	0.377
TRAVERSE Weeks 0–48	0.387	0.392	0.364	0.301	0.351	0.230
TRAVERSE Weeks 48–96	0.247	0.333	0.243	0.191	0.261	0.174
Pre-bronchodilator FEV_1, mean (SD)						
Parent study baseline	2.01 (0.65)	2.00 (0.67)	1.72 (0.50)	1.79 (0.58)	1.56 (0.47)	1.55 (0.51)
Change from PSBL to QUEST Week 52	n = 133 0.25 (0.43)	n = 263 0.36 (0.51)	n = 127 0.10 (0.38)	n = 253 0.39 (0.45)	n = 113 0.18 (0.38)	n = 193 0.34 (0.45)
Change from PSBL to TRAVERSE Week 2	n = 149 0.41 (0.46)	n = 298 0.38 (0.50)	n = 147 0.28 (0.46)	n = 288 0.37 (0.74)	n = 127 0.32 (0.39)	n = 226 0.36 (0.45)
Change from PSBL to TRAVERSE Week 48	n = 145 0.40 (0.46)	n = 288 0.43 (0.59)	n = 143 0.36 (0.47)	n = 284 0.40 (0.54)	n = 126 0.36 (0.38)	n = 213 0.36 (0.47)
Change from PSBL to TRAVERSE Week 96	n = 42 0.44 (0.48)	n = 117 0.37 (0.56)	n = 82 0.36 (0.44)	n = 160 0.32 (0.43)	n = 63 0.33 (0.40)	n = 108 0.34 (0.45)

PBO/DPL, patients treated with placebo during QUEST who switched to dupilumab during TRAVERSE; DPL/DPL, patients treated with dupilumab through QUEST and TRAVERSE.
AER, annualized exacerbation rate; FEV_1, forced expiratory volume in 1 second.

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Conflicts of interest: Busse WW: GSK, Novartis, Sanofi – consultant, speaker fees. de Mir I: GSK, Sanofi – personal fees for lectures and boards; Novartis – conference registration and travel fees; Aldo-Unión – conference registration fees. Kraft M: AstraZeneca, GSK, Chiesi, Sanofi – consultant, speaker fees; RaeSedo – co-founder and CMO. Maselli D: Amgen, AstraZeneca, GSK, Sanofi-Regeneron Pharmaceuticals Inc. – consultant, speaker fees. Domingo C: ALK, Allergy Therapeutics, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Esteve, Ferrer Pharma, GSK, HAL Allergy, ImmunoTek, Menarini, Novartis, Pfizer, sanofi-aventis, Stallergenes Greer, Takeda, Teva – travel and speaker fees. Jacob-Nara JA, Rowe PJ, Pandit-Abid N: Sanofi – employees, may hold stock and/or stock options in the company. Xia C, Soler X, Deniz Y, Sacks H: Regeneron Pharmaceuticals Inc. – employees and shareholders.

001604 | Impact of single inhaler triple therapy in asthmatic patients lung function: Experience of an allergy and clinical immunology unit

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*Presenting author: M. Areia

Background: Asthma is the most prevalent chronic respiratory disease and it bears an important burden, especially in patients with moderate to severe disease. Combination of medium or high-dose inhaled corticosteroids (ICS) and long-acting inhaled β2-agonists (LABA) is the preferred approach, but a significant number of patients with asthma remain uncontrolled despite this treatment. Adding long-acting muscarinic antagonists (LAMA) is recommended in patients aged ≥18 years. Single inhaler triple therapy (SITT) formulations with ICS/LABA/LAMA appeared as an alternative for these patients but its precise efficacy in real life is uncertain.

Method: Retrospective observational study of pulmonary function tests (PFT) of adult patients with suspected asthma performed in 2022, selecting those who had started SITT. PFT values pre and post SITT were collected, as well as sociodemographic, atopic status, and symptom control data. Data analyses were undertaken using SPSS27.

Results: We enrolled 46 patients (73.9% females, medium age 52.1 ± 15.8 years, 58.7% atopic), 3.1% of the total PFT reviewed. Forty-four patients treated with mometasone-indacaterol-glycopyrronium and 2 patients with fluticasone furoate-vilanterol-umeclidinium were included. Subjective improvement in symptom control was reported by 78.4%. The median of variation of forced expiratory volume in the first second (FEV1) was 125 (min. −510; max. 1120) mL, forced

mid-expiratory flow (FEF 25%–75%) 220 (min. −420; max. 3200) mL and Tiffeneau index 0.03 (min. −0.19; max.0.22) with statistical significance ($p < 0.001$). No significant differences were found in fractional exhaled nitric oxide (FeNO). Our patients also showed a significatively decrease in bronchodilation test after SITT initiation ($p < 0.001$). Twelve patients (26.1%) did not respond to SITT. Age, gender and atopy were not significantly associated with response. In the group of patients with response to SITT, FEV1 improved 0–99 mL in 20.6%, 100–199 mL in 29.4%, 200–399 mL in 32.4% and ≥400 mL in 17.6%. No adverse events were reported.

Conclusion: SITT showed to be safe and beneficial in lung function improvement in our patients. It may be an alternative before escalating to systemic therapies such as biologics. Besides, SITT has the potential to improve treatment adherence by reducing the number of inhaler devices and daily inhalations required for maintenance treatment. Further prospective research is needed to support recommendation for its use in asthma patients.

Conflicts of interest: The authors did not specify any links of interest.

000137 | The effects of Derp6 and Cupa1 allergens on the different cell death pathways in bronchial and nasal epithelial cells

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Hacettepe University, Ankara, Türkiye

*Presenting author: H. Akel Bilgic

Background: Pollens and house dust mites (HDM) are two of the most common allergen sources that cause allergic rhinitis and allergic asthma. Derp6, an HDM allergen with serine protease activity, causes epithelial barrier disruption and inflammatory response. Cupa1 is the major allergen of the Cypress tree (*Cupressus arizonica*), a popular ornamental plant in Mediterranean countries, and one of the most prevalent causes of seasonal respiratory allergies. There is highly restricted information on the impact of both allergens on death pathways. We aimed to investigate the effects of Derp6 and Cupa1 allergens on different cell death pathways, such as apoptosis, anoikis, necroptosis and parthanatos in nasal and epithelial cells.

Method: BEAS-2B and RPMI-2650 cells were cultured in BEGM and EMEM, respectively. Cytotoxicity and cell viability assays (MTT, LDH and live/death cell staining) were performed at 8, 24 and 72 hours after stimulation with Derp6 and Cupa1 allergens at 2, 5, 10, and 20 µg/mL. According to cytotoxicity results, 72 h was selected for further experiments. Both cells were seeded into 48-well plates and grown until 80% confluency. Cells were then stimulated with Derp6 (10 µg/mL & 20 µg/mL for both cells) and Cupa1 (2 µg/mL & 5 µg/mL for BEAS-2B; 10 µg/mL & 20 µg/mL for RPMI-2650). After incubation, the gene expressions of apoptosis (*CAS-3*, *-8*, *-9*, *BCL-2*), anoikis (*BMF*, *BIT1*, *CDH1*), parthanatos (*AIF*, *PARP1*) and necroptosis (*RIPK3*, *MLKL*) pathways were investigated by qPCR.

Results: While Derp6 stimulation increased *CAS3*, *CAS9*, *BCL2*, *BMF* and *ECAD* expression in BEAS-2B cells, 5 µg/mL Cupa1 stimulation enhanced *CAS9* and *ECAD* expression. After allergen stimulation, there is no significant increase in *CAS8* gene expression in BEAS-2B cells (Figure 1A). Meanwhile, only the increase in *RIPK3* gene expression was statistically significant in RPMI-2650 cells stimulated with 20 µg/mL Cupa1 (Figure 1B). However, no major changes in parthanatos or necroptosis-related genes were observed in each cell.

Conclusion: Depending on the allergen protease type and epithelial cell origin, allergens have a potential to stimulate different cell death pathways. Among the allergen protease-induced cell death pathways, anoikis may be a common pathway like caspase-dependent pathways.

*This study was supported by BAP (FHD-2021-19712) and TUSEB (21234)

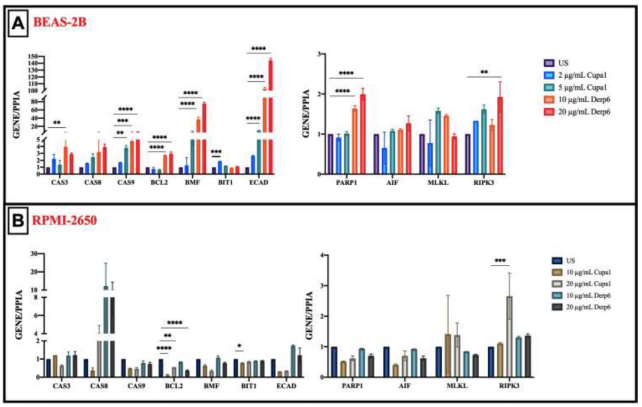

Figure 1: The effect of the Cupa1 and Derp6 allergens on gene expression associated with cell death pathways. The levels of gene expression in cell death pathways (apoptosis, anoikis, partanatos, necroptosis) in BEAS-2B (A) and RPMI-2650 (B) cells stimulated for 72 hours with different concentrations of Derp6 and Cupa1 allergen is shown. Lines indicate averages and $p < 0.05$ was considered statistically significant.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on anaphylaxis and food allergy

000456 | The basophil activation test is the best biomarker to predict severity and threshold of allergic reactions to baked egg in double-blind placebo-controlled food challenges

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*Presenting author: S. Radulovic

Background: Identifying allergic patients at risk of severe reactions and/or reacting to smaller amounts of allergen is of a great clinical importance, particularly when advising about consumption of baked egg (BE) in egg allergic children. We aimed to identify possible

biomarkers of severity and low threshold among baked egg allergic children.

Method: 150 children aged 6 months to 15 years underwent DBPCFC to baked egg, skin prick testing and blood collection for serology and basophil activation test (BAT). Severity of allergic reactions was classified according to the Practall guidelines and threshold of reactivity determined as the cumulative dose of egg protein tolerated.

Results: 60 children reacted to BE on DBPCFC. Cutaneous manifestations were the most common, followed by gastrointestinal. 23 (38%) of BE allergic had severe reactions. Thirteen (22%) were treated with intramuscular adrenaline, and 3/13 received 2 doses. There were no statistically significant differences between severe and non-severe reactors or low / high threshold patients with regards to age, gender, ethnicity, prevalence of other atopic co-morbidities, previous symptoms following exposure to egg, skin prick test, specific IgE to egg, egg white or ovalbumin, specific IgG4 or IgG4/IgE ratios. Severe reactors had higher levels of IgE to ovomucoid (p = 0.009) and BAT to BE (p = 0.001). Patients with lower threshold had higher specific activity (i.e. egg-white-sIgE/total IgE, p = 0.027) and BAT to egg white (p = 0.007) but lower severity score (p = 0.008). Optimal cut-offs for ovomucoid-sIgE and BAT had 100%/76% sensitivity, 35%/74% specificity and 60%/75% accuracy to identify severe reactors. Optimal cut-offs for specific activity and BAT had 70/70% sensitivity, 68%/72% specificity and 69/71% accuracy to identify low threshold patients.

Conclusion: BAT was the best biomarker to predict severity and threshold of allergic reactions to BE in BE allergic children. This can be useful when making decisions about practical management of egg allergy and when considering possible immunomodulatory treatments.

Conflicts of interest: Dr. Santos reports grants and personal fees from Medical Research Council; grants from Asthma UK, Immune Tolerance Network/National Institute of Allergy and Infectious Diseases (NIAID, NIH), Food Allergy Research and Education (FARE), BBSRC and Rosetrees Trust; personal fees from Thermo Scientific, Nutricia, Infomed, Novartis, Allergy Therapeutics, Buhlmann, as well as research support from Buhlmann and Thermo Fisher Scientific through a collaboration agreement with King's College London.

000441 | Wheat-dependent exercise-induced anaphylaxis (WDEIA) affecting recreational athletes

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*Presenting author: V. Faihs

Background: In wheat-dependent exercise-induced anaphylaxis (WDEIA), allergic symptoms occur when wheat ingestion is combined with augmenting cofactors. As exercise is the most common cofactor in this disease, we aimed to analyse the clinical characteristics and the disease burden in recreational athletes suffering from WDEIA.

Method: 15 patients with WDEIA diagnosed by oral challenge test with weekly exercise routine were included. Clinical and serological characteristics as well as questionnaires were retrospectively analysed and completed with phone interviews for follow-up.

Results: 5 female and 10 male WDEIA patients with a median age of 39 years and a median exercise frequency of 3 times per week were included. In most cases, many years (median 4, range 0.5–24) passed from the first allergic reaction to the diagnosis, leading to a high number of allergic episodes (median 17.5), ranging from only urticaria to severe anaphylaxis. In 93% of patients, symptoms had always started during exercise, only in one case after exercise cessation. Endurance exercise elicited reactions in all patients, while 47% reported that weight training had never led to symptoms. In 53%, exercise was the only known cofactor in the patients´ histories. However, for diagnosis, in 87% of patients, in the provocation test reactions could already be elicited with high doses of wheat gluten alone or in combination with acetylsalicylic acid (ASA); just in 2 cases additional exercise was needed as a cofactor. After their first allergic reaction, a significant loss of quality of life (QOL) was described (p < 0.01). Out of fear, 6 patients reduced, and 1 completely stopped their exercise routine. The diagnosis and education could return the patients a substantial amount of QOL (p < 0.05 vs. before diagnosis; n.s. vs. before first reaction). After a median follow-up of 18 months, no severe reactions occurred. 40% of patients remained reaction-free, while the rest experienced single episodes with mild urticaria.

Conclusion: In recreational athletes suffering from WDEIA, diagnosis is often delayed by many years, leading to numerous allergic reactions and severe impairment of QOL. Even if exercise is the primary cofactor in the patients´ history, diagnosis can often be confirmed by wheat gluten +/- ASA provocation test. With the correct diagnosis and patient education, patients can return to their exercise routine without experiencing severe allergic reactions, and thus restore most of their former QOL.

Conflicts of interest: The authors did not specify any links of interest.

001463 | Mast cell activation test, a novel approach for cow's milk food allergy diagnosis in children

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*Presenting author: R. Bahri

Background: The main effector cells in IgE-mediated food-induced allergic reactions are basophils and mast cells (MCs). Conventional allergy tests (skin prick testing, serum allergen-specific IgE) have limitations in terms of sensitivity and specificity; the basophil activation test may be more accurate but is technically challenging and thus limited to a few specialist centres. We have previously reported a novel *in vitro* diagnostic using patient sera, the mast cell activation test (MAT), for peanut allergy, and now seek to apply this to cow's milk (CM) allergy.

Method: We generated human primary mast cells (MCs) from peripheral blood CD117$^+$ haematopoietic progenitors. Cells were cultured in serum-free media until differentiation. An activation test using IgE/anti-IgE stimulus was used to confirm MC maturity. CD117+ and FcεRI membrane expression were checked using flow cytometry. Mature MCs were passively sensitized overnight with 10 sera from (i) CM-allergic children who had undergone positive food challenges or (ii) non allergic patient control sera. The next day, sensitized MCs were stimulated with increasing doses of allergen (fresh CM). MAT response was assessed by measuring up-regulation of surface CD63 and CD107a using flow cytometry. We validated a bar-coding system, where six different conditions for a single patient could be run as a single sample on the flow cytometer. The release of the granule protease β-hexosaminidase was measured in collected supernatants.

Results: After 8–10 weeks of cell culture, MCs were pure, fully granulated tryptase$^+$chymase$^+$ (≥90%), able to bind IgE at their surface and responded highly to the FcεRI engagement (60%–90%). MCs passively sensitized with sera from milk-allergic donors degranulated in a dose-dependent manner to fresh CM. Different patterns of MAT response were identified, which correlated to clinical data.

Conclusion: Milk MAT shows a dose-dependent and significant response to CM allergens, and can therefore be considered a tool to aid the diagnosis of CM allergy. Compared to existing allergy diagnostics, MAT may be useful to explore differences in effector cell function between basophils and MCs during allergic reactions.

Conflicts of interest: The authors did not specify any links of interest.

000062 | Knowledge of anaphylaxis management and AAI administration among parents of children with food allergies: A cross-sectional study

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*Presenting author: C. Cronin

Background: Anaphylaxis is a severe, life threatening allergic reaction involving multiple body systems. The incidence of anaphylaxis is highest in the first decade of life, while mortality resulting from anaphylaxis is highest in the second decade of life.

Intramuscular adrenaline with an adrenaline autoinjector (AAI) is the first-line therapy for anaphylaxis. However, many patients and caregivers are often unable to demonstrate correct administration of their prescribed AAI. This may reflect several issues including training effectiveness, user stress during administration or inherent differences of the individual brand of auto injector.

Currently, no studies have assessed the parental knowledge of anaphyalxis management and AAI use in Ireland.

Aim: The aim of this study is to assess the knowledge of anaphylaxis management and adrenaline auto injector use among caregivers of children with food allergies.

Method: This was a cross sectional study which took place in the paediatric allergy clinic at Cork University Hospital, Ireland. Parents of children with food allergies who were prescribed an AAI completed an online questionnaire regarding anaphylaxis management and were assessed in the use of their child's AAI via a video call.

Results: 185 parents completed the online questionnaire. Of these, 66% (124) parents had not received training in AAI administration in the past 12 months, while 57.8% (107) had not received training in anaphylaxis management in the past 12 months. Parents had good overall knowledge of the definition of anaphylaxis (91%), the management of allergic reactions involving the skin (92.1%) and the management of anaphylaxis with respiratory symptoms (86.5%). However, parents were less informed of the management of cardiovascular and gastrointestinal symptoms of anaphylaxis (50.2%). There was an association observed between anaphylaxis knowledge and the age of the parent ($p = 0.008$).

150 parents were assessed in their ability to use their child's AAI., 32.6% (49) were able to identify all 5 steps of AAI administration. Of these, three steps were identified as being essential for successful adrenaline administration. 40 parents (26.6%) deminstrated all three steps correctly, this was largely due to failing to identify to push in and hear a 'click' from the device (64.6%).

Conclusion: This is the first study in Ireland to assess caregiver knowledge of anaphylaxis management and AAI administration. Parents had a good overall knowledge of anaphylaxis management, however, the ability to explain the use of an AAI was suboptimal. There is a need to create comprehensive and accessible anaphylaxis management education for parents. Further trials should be conducted to evaluate the effectiveness of remote and accessible educational interventions for parents of children with food allergies. This study supports the EAACI recommendation of Reinforcement of anaphylaxis management knowledge and AAI use with revision at regular intervals for parents and patients, which helps patients feel more knowledgeable and confident about managing triggers and responding in an emergency.

Conflicts of interest: The authors did not specify any links of interest.

000089 | Anaphylaxis at diagnosis and progress on the egg ladder

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*Presenting author: A. Gallagher

Background: Egg allergy is the second most common food allergy in children and one of the main causes of anaphylaxis in infants. Recent

studies have shown that the early stepwise introduction of egg to the diet can promote earlier tolerance. In Ireland reintroduction of egg to the diet is reached following home-based induction of egg protein via the egg ladder. Seemingly the longer the egg allergy persists the less likely the child will achieve tolerance; therefore early introduction is imperative.

Method: A sample of 300 charts of children with symptoms of anaphylaxis to egg at diagnosis in the paediatric clinic in Cork University hospital from 2011 to 2021 were reviewed. Inclusion and exclusion were applied. Data were analysed using STATA.

Results: 300 charts were reviewed, 78 were excluded due to Skin Prick Test (SPT) <3 mm (*n* = 222). 40 children had symptoms of anaphylaxis at diagnosis. 7 are currently ongoing treatment and 8 were lost to follow up. 20 children achieved tolerance (80%) and 5 suspended treatment and are now avoiding egg in some form. Reasons for suspending treatment included; parental anxiety (*n* = 2), other medical condition (*n* = 1), behavioural issues (*n* = 1) and frequent reactions (*n* = 1). Only 1 child had symptoms of anaphylaxis due to accidental exposure and no children had anaphylaxis while consuming steps of the egg ladder. Average time on the ladder was 34.1 months, approximately 4 months longer than the overall average. Average age at diagnosis was 13.5months and average age at start of treatment was 26.67months. 19 were carrying adrenaline autoinjectors.

Conclusion: Home based introduction of egg protein via the egg ladder is safe and effective, even in children with symptoms of anaphylaxis at diagnosis.

Conflicts of interest: The authors did not specify any links of interest.

001378 | How common are allergic reactions during commercial flights?

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*Presenting author: J. Mamula

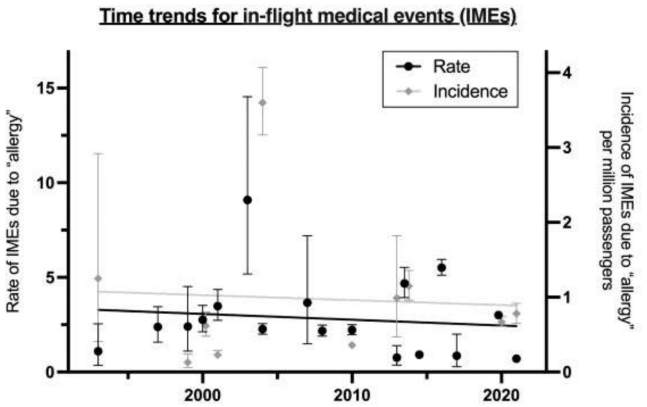
Background: Global passenger demand for air travel has increased by over 7% annually since 2006. Passenger numbers are now recovering following COVID-19 back to pre-COVID levels. Prior to COVID-19, individuals with food allergies reported significant concern and anxiety over the risk of reactions when travelling by air. However, reported rates of in-flight medical events (IMEs) secondary to allergic reactions are limited.

We conducted a systematic review with meta-analysis to estimate the incidence of IMEs due to allergic reactions on commercial flights.

Method: We searched the Medline, Embase, Transport and Cochrane databases for publications since 1980 reporting in-flight medical emergencies of allergic aetiology, using a search strategy previously published [Borges do Nascimento et al. doi: 10.1016/j.ajem.2021.04.010]. We assessed risk of bias, and extracted relevant data for meta-analysis using R. We also assessed time-trends in both rate and incidence of allergic reactions using logistic regression. Registered at PROSPERO (CRD42022384341).

Results: A total of 17 publications met inclusion criteria. At meta-analysis, a pooled estimate of 2.2% (95%CI 1.6%-3.1%) of IMEs are coded as being due to allergic reactions. This may be higher in children (3.1%, 95%CI 1.5%–6.7%). There was no evidence to suggest a change in the proportion of IMEs due to allergic reactions over time. The incidence of allergic IMEs was estimated at meta-analysis to be 0.7 events per million passengers (95%CI 0.4 to 1.1), again with no evidence suggesting a change in incidence over time.

Conclusion: Allergic reactions coded as IMEs during commercial air travel are uncommon, occurring at an incidence around 400-times less than that reported for accidental allergic reactions to food occurring in the community. Furthermore, there is no evidence of a change in incidence of allergic IMEs in the last 3 decades.



Conflicts of interest: The authors did not specify any links of interest.

001042 | Increased MIR-21-3P and decreased MIR-375-3P levels within circulating extracellular vesicles from children with anaphylactic food-induced reactions

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*Presenting author: E. Nuñez-Borque

Background: Extracellular vesicles (EVs) and microRNAs (miRNAs) are starting to gain relevance in the underlying molecular mechanisms of anaphylaxis. Our previous studies showed differential expression levels of miR-21-3p, miR-487b-3p and miR-375-3p in serum from children with food anaphylaxis. This study aimed to evaluate

the involvement of these EVs-derived miRNAs in human anaphylactic reactions.

Method: EVs were purified from serum samples collected within the first 30 minutes from the onset of the reaction (acute phase) and 14 days later (baseline phase) of 15 food-induced anaphylactic children. Isolated vesicles were characterized by immunodetection of EV markers, electron microscopy and nanoparticle tracking analysis. Then, miRNAs of interest were extracted from isolated EVs, retrotranscribed and quantified by qPCR. In addition, we performed an *in silico* system biology analysis (SBA) on their target genes. Among the different categories provided, "disease and disorders" and "canonical pathways" were considered to study.

Results: A population of vesicles with a diameter around 100 nm was properly purified, however we did not found size or concentration differences between acute and basal EVs. Three out of 15 patients were discarded from the study due to acute and/or basal serum hemolysis. miR-487b-3p determinations did not show variation in their levels between acute and baseline samples. However, miR-21-3p was significantly increased (*$p = 0.0269$) and miR-375-3p was significantly decreased (**$p = 0.0015$) in EVs obtained during the acute phase compared with those in the baseline. Furthermore, the SBA revealed several diseases and biologic processes closely related to the pathophysiology of anaphylaxis, such as cell degranulation, immune response activation, inflammation, increase of endothelial permeability and vasodilation.

Conclusion: This study provides, for the first time, a differential miRNA expression profile within circulating EVs from anaphylactic patients. Moreover, the *in silico* study revealed a possible implication of these molecules in the underlying molecular mechanisms.

Conflicts of interest: The authors did not specify any links of interest.

000096 | Increasing incidence of anaphylaxis and specific characteristics in very early childhood- an area which needs to be highlighted

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Background: Rising rates of anaphylaxis have been noted worldwide. However, studies focusing specifically on presentations in very early childhood (<2 years of age) are lacking. We aimed to investigate changes in the incidence of anaphylaxis in infants and young toddlers over a 15-year period and explored clinical signs, symptoms and management in <2 year old children.

Method: In this observational study we retrospectively analysed patients aged <2 years, presenting to Western Australia's sole tertiary paediatric Emergency Department (ED) with a coded diagnosis of anaphylaxis. We assessed presentations over two time periods (2003–2007 and 2013–2017). In manually confirmed cases, comorbidities, triggers, symptoms, and management were recorded.

Results: We demonstrated a 1.7-fold (OR 1.88; 95%CI 1.42–2.51; $p < 0.001$) rise in incidence of confirmed cases of anaphylaxis between the two time periods. A greater increase (1.9-fold) was seen in those aged <1 year (OR1.95; 95%CI 1.36–2.81; $p < 0.001$). Comorbidities, triggers, and symptoms were not different over time. 91.6% (219/239) presented with respiratory, 43.1% (103/239) with gastrointestinal, 40.6% (97/239) with neurological and 23.4% (56/239) with cardiovascular symptoms. A history of atopic dermatitis was present in 56.1% of cases, whilst 43.5% had a history of food allergy, 13.8% had a history of wheeze, and 18.8% of patients presented with an intercurrent illness. Appropriate management with adrenaline improved over time ($p = 0.007$) and oral antihistamines and steroids were appropriately less administered ($p = 0.013$).

Conclusion: The incidence of ED anaphylaxis presentations in very early childhood increased significantly within a 15-year period. A further rise likely will occur in tandem with ongoing environmental changes. However, children <2 years present with signs which are not recognised within internationally accepted definitions and guidelines. Physicians and caregivers need to be aware of specific characteristics in this nonverbal age group to provide timely recognition and optimal management and guidelines.

Conflicts of interest: The authors did not specify any links of interest.

001169 | Study of A-gal glycosylation of cow's milk proteins and allergological implications

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Background: Alpha gal syndrome (AGS) is a mammalian meat allergy associated with tick bites and specific IgE antibodies to the oligosaccharide galactose-α-1,3-galactose (α-gal). The α-gal epitope is abundantly expressed on glycolipids and glycoproteins from non-primate mammals, but not in humans, where the gene encoding α-1,3-galactosyltransferase is not functional. AGS shows several exclusive features that make it different from common food allergies: (i) it is characterized by late on-set symptoms, appearing 3 to 6 hours after mammalian meat consumption; (ii) IgE antibodies are against a carbohydrate moiety rather than a protein epitope; (iii) patients can develop AGS in late adulthood. The symptoms ranged from gastrointestinal diseases, urticaria, angioedema, to anaphylaxis. Commins et al. (2016) demonstrated that not only red meat, but also bovine

milk, might contain α-Gal-epitopes. In more recent studies, in fact, the 10–20% of AGS patients even react to milk. Combining the recent findings of Perusko et al. (2020) about milk involvement in AGS and the considerations of Román-Carrasco et al. (2019), about the role of lipids in eliciting α-Gal reaction, we investigated the milk fat globule protein (MFGP) fraction, to discover α-Gal carrying proteins and to evaluate their immune-recognition by AGS patients.

Method: The milk protein fractions including Milk Fat Globule Proteins (MFGP) were extracted from fresh cow's milk and separated by LDS-PAGE under reducing condition. The use of magnetic beads was useful to obtain a successful purification of the α-gal glycosylated proteins. The anti-α-Gal monoclonal antibody and the serum of 10 patients with a documented α-gal syndrome were tested by immunoblotting and the extracted proteins were identified by means of LC-HR MS/MS.

Results: The immunoblotting showed that the MFGP fraction is α-gal glycosylated. Both the anti-α-Gal monoclonal antibody and the IgE of patients with α-Gal syndrome showed reactivity towards a high molecular weight protein (>200 kDa).

Conclusion: With the first results obtained from LC-MS/MS identifications, it seems that the high molecular weight protein could be an aggregate of at least two different proteins recognized by the AGS patients' IgEs.

These results suggest that it is important to investigate further the risk associated to milk consumption for patients suffering from α-Gal syndrome.

Conflicts of interest: The authors did not specify any links of interest.

001465 | Teaching children with food allergy to recognise anaphylaxis: The caregivers' perspectives

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Background: Anaphylaxis is rising in prevalence amongst children. The current recommendations on the effective transition of anaphylaxis management to adolescents and young adults includes starting transition at 11–13 years of age. However, few researchers have investigated the perspective of caregivers regarding transition of anaphylaxis management to their children. This study aims to determine at what age caregivers believes children should learn to recognise anaphylaxis and use their AAI.

Method: Caregivers of paediatric allergy patients were contacted by phone and invited to complete a questionnaire about when they begin to transfer these responsibilities from caregivers to children and adolescents.

Results: Of the 123 responses to the questionnaire received, 44.7% indicated that 9–11 years was the appropriate time for teaching their children to self-inject an AAI. History of severe anaphylaxis (94.3%), child's ability to describe reasons to inject adrenaline (87.8%) and demonstrate AAI use (82.1%) were "very important" readiness factors identified. Almost half of caregivers were "not confident" (8.94%) or "somewhat confident" (40.65%) in training their child to use AAI. Caregivers with higher household incomes more frequently identified themselves as the party responsible for training their children to use AAI ($p = 0.04$).

Conclusion: Caregivers begin to transfer the responsibility of anaphylaxis recognition and AAI use to their children significantly younger than the EAACI recommended age of 11–13 years. Caregivers expressed suboptimal confidence in teaching their children to use AAI. Further evaluation is necessary to improve guidelines, enabling clinicians to train and support caregivers during this transition.

Conflicts of interest: The authors did not specify any links of interest.

001538 | The effect of adrenaline autoinjector use on patients with anaphylaxis

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Background: Adrenaline is the most important treatment of anaphylaxis. It is recommended to prescribe an adrenaline autoinjector (AOE) to every patient at risk of anaphylaxis in all guidelines. As the frequency of AOE use increases, misuses also increase, which may lead to failure in the treatment of anaphylaxis. In this study, we aimed to investigate the compliance of patients with AOE use and their ability to apply AOE.

Method: A total of 112 patients (52 women and 60 men, aged 18–60 years) who were prescribed AOE for various anaphylaxis reasons, were included in the study. First these patients were applied a questionnaire about AOE use and compliance and were asked to show us the use of AOE with a demo. The mistakes of the patients during this application were determined.

Results: AOE was prescribed to patients for various anaphylaxis reasons such as bee venom allergy (BVA) ($n = 77$), food allergy ($n = 14$), drug allergy ($n = 4$), latex allergy ($n = 3$), and idiopathic ($n = 14$). When the survey results were evaluated, it was determined that the patient group with BVA took the use of AOE more seriously and used the AOE more accurately. Also the patients in the 20–40 age group used AOE more accurately and faster, and the female patients used AOE more faster than the male patients. Most of the patients had difficulty in the 3rd step (unlocking the AOE).

Conclusion: It cant be predictable where, when and how anaphylaxis will develop and how it will progress. The most important treatment for anaphylaxis is rapid and proper administration of adrenaline. In this study, we determined that some of the patients could not remember the use of AOE exactly and could not use their AOEs

appropriately and effectively during a possible anaphylaxis attack. That's why these patients were reminded that the more properly and quickly AOE is used, the less life-threatening risk will be happen. As a result, patients who were previously prescribed AOE should be invited for control visits at various periods and verbal and visual information should be given to them about the use of AOE even if they have been already taught.

Conflicts of interest: The authors did not specify any links of interest.

000312 | Elicitor-specific phenotypes and factors of food-induced anaphylaxis: Data from the European anaphylaxis registry

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*Presenting author: S. Dölle-Bierke

Background: Food is one of the most common elicitors of anaphylaxis with the potential to cause life-threatening allergic reactions. The aim of this study was to characterize phenotypes and factors of food-induced anaphylaxis (FIA) in an elicitor-specific manner.

Method: Cases of confirmed FIA from the Network for Online Registration of Anaphylaxis (NORA) were analysed. Association analyses (Cramer's V) and risk assessment (odds ratio, OR) were performed in an age- and sex-dependent approach with respect to symptom profile, atopic comorbidities, recurrent reactions and augmentation factors like exercise.

Results: We identified 3427 cases of confirmed FIA showing an age-dependent elicitor ranking with five main food allergen sources in children (peanut, cow's milk, cashew, hen's egg and hazelnut) and a different, but also broader range of elicitors in adults. Characteristic symptom patterns were identified for wheat and cashew. In wheat anaphylaxis more cardiovascular symptoms were presented (75.7% vs. 49.0%; Cramer's V 0.28) and in cashew anaphylaxis more gastrointestinal symptoms (73.9% vs. 54.9%; Cramer's V 0.20), each compared to the reference food group. Concomitant atopic dermatitis was weakly associated with anaphylaxis to hen's egg (Cramer's V 0.19) and exercise was strongly associated with wheat anaphylaxis (Cramer's V 0.56), however severity was not associated with these factors. Interestingly, accompanied alcohol intake in wheat anaphylaxis (OR: 3.23, CI. 1.31–8.83) and exercise in peanut anaphylaxis (OR: 1.78, CI: 1.09–2.95) were significantly linked with severe reactions.

Conclusion: Overall FIA is a unique allergic manifestation, which is to a great extent age-dependent. Individual food allergens show rather overlapping than distinguished symptom and severity profiles.

Conflicts of interest: The authors did not specify any links of interest.

000420 | Detection of JUG R 1-specific IGE in 0–2-year-old children with sensitization to hen's egg, cow's milk, or wheat

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Background: In recent years, tree nut allergy in children has been increasing, with walnuts being the most common in Japan. Allergic reactions, including anaphylaxis, frequently occur at the first intake of the tree nuts, suggesting the children have been sensitized before that. However, there are few studies on the sensitization to tree nuts in infants considered to be high-risk. On the other hand, many studies have reported a high diagnostic performance of specific IgE (sIgE) test to Jug r 1, the representative allergen component of walnut.

Method: 0–2-year-old children who had a positive sIgE to egg white, milk, or wheat and had never ingested walnuts were screened for Jug r 1-sIgE between November 2018 and December 2022. The clinical background for age, sex, complications of other allergic diseases, confirmed egg, milk, or wheat allergy (diagnosed by a definitive history of immediate reaction or positive oral food challenge test), and the status of walnut consumption as of December 2022 were examined retrospectively.

Results: The Jug r 1-sIgE positivity rate (> 0.34 kUA/L) of 205 subjects (125 males) was 9.8% (20/205), with a median Jug r 1-sIgE of 12.5 kUA/L (range 0.41–508) in positive subjects. Complication of atopic dermatitis (AD) was observed in 119 subjects (58%), and Jug r 1-sIgE positivity was significantly higher in the AD+ group (15.1%

[18/119]) compared with AD- group (2.3% [2/86], p = 0.001). Jug r 1-sIgE positivity by sensitized antigen was 13.7% (14/102) for egg, 17.0% (8/47) for milk, and 17.1% (7/41) for wheat in the AD+ group, whereas it was 2.9% (2/68), 3.4% (1/29), and 0% (0/13), respectively, in the AD- group. In the subjects with confirmed food allergies, Jug r 1-sIgE positivity in the AD+ group was 14.5% (11/76) for egg, 17.8% (8/45) for milk, and 17.9% (5/28) for wheat, whereas it was 4.3% (2/46), 4.8% (1/21), and 0% (0/12), respectively, in the AD- group. Regarding the age at examination, Jug r 1-sIgE positivity was 5.9% (1/17) at age 0, 8.5% (9/98) at age 1, and 11.1% (10/90) at age 2, whereas it was 10.0% (1/10), 14.8% (8/54), and 16.4% (9/55), respectively, in the AD+ group. Among the Jug r 1-sIgE positive subjects (n = 20), one was able to ingest a small amount of walnuts, but the others had not ingested walnuts yet as of December 2022.

Conclusion: In 0–2-year-old children sensitized to egg, cow's milk, or wheat, 9.8% were sensitized to Jug r 1. Moreover, the Jug r 1-sIgE positivity rate was above 15% in subjects with AD complication. These children could be considered to perform a component-screening test to prevent unexpected anaphylaxis at their first intake.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on allergen Immunotherapy I

001540 | Peanut oral immunotherapy in a tertiary pediatric allergy unit

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Background: For children with peanut allergy, peanut avoidance is the standard of care. Oral immunotherapy (OIT) with Peanut (Arachis hypogaea) Allergen Powder-dnfp (PTAH), an oral biologic drug approved by the Food and Drug Administration and the European Commission, seems a promising treatment. However, it is not available everywhere and more studies are needed regarding patient selection and expected outcomes for peanut OIT. The aim of this study is to show OIT results in terms of safety, efficacy, feasibility and expected outcomes by using salty peanuts as food product in a real-world peanut OIT effort in children. Moreover, to define differences, if any, in the outcomes of peanut OIT in different age groups.

Method: We reviewed records of children allergic to peanut and undergoing peanut OIT at the Allergy Unit of Meyer Children's University Hospital IRCCS from May 2021 to May 2022. Demographic, clinical and allergological features were collected for correlation with peanut OIT outcomes, as well as information about reactions during OIT and time to complete dose escalation.

Results: 56 patients aged 22 to 209 months (mean age 102.3 ±48.6 months) and with peanut allergy were treated with peanut OIT. 8/56 (14.3%) patients were <4 years. 15/56 (26,8%) children completed escalation in a mean time of 16.4 ±11.0 months and were fully desensitized to 3500 mg of peanut (710 mg of peanut protein); of these, 13/15 (86.7%) were >=4 years and 2 (13.3%) were <4 years. Among the remaining 41 patients, 36 (87.8%) were still undergoing OIT with mean maintenance dose of 416.8 mg ±437.4 mg; of these, 5 patients (13.9%) were <4 years. Five out of 41 (12.2%) patients interrupted OIT because of frequent mild reactions, and one of these was <4 years. 30/56 patients (53.6%) experienced reactions during dose escalation, 8/30 (26.7%) at home and 22/30 (73.3%) at the hospital. Most reactions were mild and only 9/30 (30%) patients required therapy, of whom only two (6.7%) needed treatment with epinephrine. In particular, 26/48 patients aged ≥4 years (54.2%) and 3/8 aged <4 years (37.5%) experienced a reaction during OIT.

Conclusion: Peanut OIT increased the tolerance threshold in most patients, only 5 (8.9%) discontinued due to poor compliance. It can be conducted in all age groups since the reactions occurring at controlled doses are usually mild and self-limiting. Reactions during peanut OIT seem more frequent in older patients, but further studies are needed in a larger cohort to investigate differences in outcomes between older and younger children.

Conflicts of interest: The authors did not specify any links of interest.

001644 | Road to oral immunotherapy for all food allergic infants: Design of the Orka-NL study

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*Presenting author: T. Klok

Background: Recent studies suggest that oral immunotherapy is associated with long-term tolerance development in food allergic children, but only when started early in life. Currently, just one randomized controlled trial is performed, only including children with a peanut allergy.

Method: From 2019 to 2023 we performed a safety and feasibility study on early oral immunotherapy (e-OIT) for children 9–24 months of age with a food allergy. Over 100 children received oral immunotherapy (1-year, daily 300 mg protein) for different kind of food allergies, including therapy for multiple allergies. The limited side effects, the feasibility of the therapy for most children and the current rate of sustained unresponsiveness of 80% (no control group included) are comparable with data from studies on peanut e-OIT.

Therefore, we hypothesize that e-OIT in young children with an established food allergy will induce long-term tolerance within one year in at least 50 percent of children with a persistent allergy. For example, in children with peanut-allergy we expect a rate of 80% persisting allergy in the routine care group (strict avoidance of the allergen). The hypothesized outcome after 1 year e-OIT is 60% long-term tolerance (40% (half of 80%) + 20% spontaneous tolerance).

Results: In 2023 we started a multi-center, randomized controlled superiority trial. 500 children between 9 and 30 months old with an IgE-mediated food allergy to peanut (n = 60), tree nuts (n = 180),

cow's milk (n = 150) and/or hen's egg (n = 110) as proven by an oral food challenge will be included. Intervention is 1-year low-dose oral immunotherapy for up to 4 allergens (daily 300 mg allergenic protein) compared to strict avoidance in the control group.

Main study endpoint is sustained unresponsiveness, defined as passing an exit oral food challenge at 4 weeks after discontinuation of the 12 months oral immunotherapy, and uncomplicated consumption of a full dose of the specific food at home, after 6 months unrestricted introduction of the specific food into the diet.

Conclusion: Single and multiple e-OIT is a very promising treatment for all young food allergic children. The presented study will provide valuable knowledge on the effectiveness of the therapy, and may contribute to an era with e-OIT as standard therapy for food-allergic infants.

Conflicts of interest: The authors did not specify any links of interest.

100045 | House dust mite sublingual immunotherapy liquid formulation for treating patients with allergic rhinitis: A systematic review and meta-analysis of randomised and nonrandomised studies

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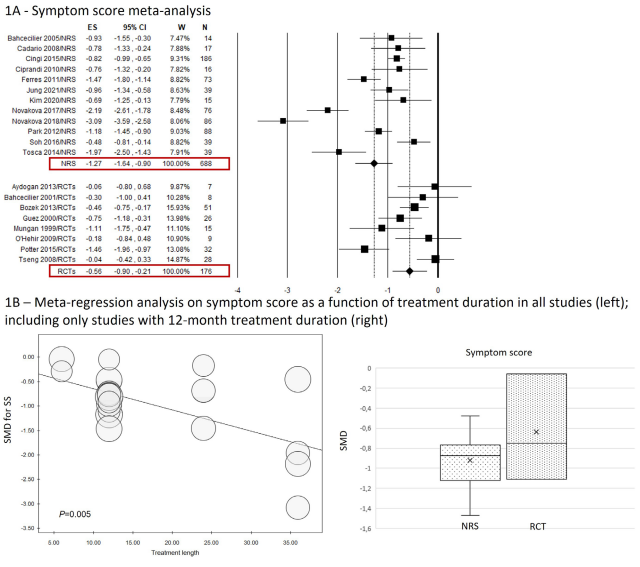
Background: If randomised controlled trials (RCTs) are the gold-standard of evidence in allergen immunotherapy (AIT), nonrandomised studies (NRS) help to confirm results in a broader and more representative population, considering personal modalities of use in routine practice. However, discrepancies may arise from NRS methodological/design limitations, but also from other sources such as long-term treatment, co-prescription with an interactive drug, poor adherence or non-persistence with drug. To explore this issue, we evaluated the benefit of sublingual AIT (SLIT) in NRS vs. RCTs focusing on a single product/allergen to reduce heterogeneity.

Method: For the meta-analysis, house dust mite (HDM) SLIT liquid (Stallergenes Greer, Antony, France) studies were sourced from computerised (MEDLINE, ISI Web of Science, LILACS databases, up to December 2022) and manual literature searches. After extraction by 2 independent observers, populations, treatments and outcome data were combined (DerSimonian-Laird method). Noncomparative NRS were compared to RCTs SLIT arm before and after treatment. Treatment efficacy was determined as the standardised mean difference (SMD) in symptom score (SS) and medication score (MS). According to guidelines by Cohen[1], effect sizes of 0.2, 0.5 and 0.8 correspond to small, medium, and large effects, respectively.

Results: SS data were available from 12 NRS (N = 688)/8 RCTs (N = 176) and MS data from 6 NRS (N = 252)/7 RCTs (N = 160). With regards to SS, the benefit with HDM SLIT was found significant in both NRS and RCTs and even remarkable in NRS (SMD −1.27, $CI_{95\%}$ [−1.64, −0.90]; Fig. 1A). Similar findings were observed for the MS with SMD equal to −1.35, $CI_{95\%}$ [−1.77, −0.93] and −0.46, $CI_{95\%}$ [−0.67, −0.25], respectively. No publication bias was evidenced. Meta-regression analysis showed that symptom improvement was correlated to the treatment duration (Fig. 1B left) with consistent results in NRS and RCTs with 12-month SS data: −0.87; IQR [−1.03, −0.77] and −0.75; IQR [−0.93, −0.41], respectively (Fig. 1B right). The results were irrespective of yearly dose, patient age, asthma and sensitisation profile, study design and sample size.

Conclusion: This meta-analysis showed a significant clinical benefit of HDM SLIT increasing over time in both NRS and RCTs, suggesting NRS may reliably integrate RCT results and be considered for inclusion in guidelines. The relevant results of NRS in the less selected population in real life better reflect the benefit that may be expected in routine care.

1. Cohen J. Statistical Power Analysis for the Behavioral Sciences (2nd ed.) Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.



Conflicts of interest: S Scurati is an employee of Stallergenes GreerJ Cognet-Sicé is an employee of Stallergenes GreerGW Canonica reports having received research grants as well as being lecturer or having received advisory board fees from: A.Menarini, Anallergo, Allergy Therapeutics, AstraZeneca, Chiesi Farmaceutici, Faes, Firma, Genentech, Guidotti-Malesci, GlaxoSmithKline, Hal Allergy, Innovacaremd, Novartis, OmPharma, RedMaple, Sanofi-Aventis, Sanofi-Genzyme, Stallergenes Greer, Uriach Pharma, ThermoFisher, Valeas D. Di Bona reports having received fees from Stallergenes Greer.

100070 | Cat allergy treated with monomeric allergoid in routine medical care: One-year observational data

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Background: Allergen immunotherapy is a potential disease modifying treatment for patients with cat allergy, but a limited body of evidence exists for SLIT and has shown mixed results in terms of clinical response. Monomeric allergoids take advantage of reduced IgE binding properties and produce limited allergic side effects.

Method: A longitudinal prospective, non-interventional, multicentre observational study was conducted in Germany from May 2021 to September 2022 to evaluate in a systematic way the short-term changes in quality of life, upper and lower airways symptoms, asthma control, concomitant medications, tolerability, and patterns of use of monomeric allergoid in tablets or drops for patients ≥ 5 years with cat allergy. Regular visits during the period were carried out according to routine medical care and assessment were done at T1 (3–4 months), T2 (5–8 months), T3 (9–14 months). The study was approved by ethical committee and followed national regulation.

Results: Evaluable subjects (mean age 33.74 years) with at least 6 months of treatment were 61. Asthma and rhinoconjunctivitis (ARC) affected 18 and 50 subjects, respectively. Most subjects used tablet formulation and followed the proposed daily or twice/weekly schedule. Satisfaction rate was good or very good in 98% of subjects at T2. At T3, RQLQ and VAS significantly improved of 50% and 75%, respectively. ARC and bronchial symptom/medication scores improved of 50% and 53%, respectively. Asthma was controlled by 44% of subjects at T0 and by 89% at T3. ARC was uncontrolled according to categorical VAS assessment by 65% at T0 and by 15% at T2. A prolongation of the time to development of symptoms was seen in 67% of subjects at T3. Tolerability was good or very good in all subjects. Six subjects reported adverse events and three discontinued the treatment for this reason.

Conclusion: Monomeric allergoid appears safe and in a considerable proportion of patients with ARC and asthma due to cat allergy shows rapid significant perceived improvement in routine medical care.

Conflicts of interest: Employment in Lofarma spa.

100172 | Immunological characterization of basophil compartment and humoral responses in a prospective open label of very low dose multi-nut oral immunotherapy

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Background: Tree nut and peanut allergies are the most common causes of anaphylaxis in childhood and allergies to multiple nuts are common. Oral immunotherapy (OIT) is provided in specialized centres as a treatment for food allergies with medium to high maintenance doses ≥ 300 mg protein/allergen. This is associated with a high rate of side effects, making OIT to multiple foods extremely difficult. Very low dose OIT (VLOIT) to multiple foods may increase the safety and feasibility profile while maintaining efficacy. The aim of this study is to investigate changes in basophil activation and allergen specific IgE titers in a multi-nut VLOIT.

Method: Eighteen children with oral food challenge-confirmed allergy to 2–5 tree nuts and peanuts were enrolled in Very Low Dose Multi-OIT study (NCT03799328). Whole blood and serum samples were collected at baseline, when the maintenance dose was achieved (~30 mg protein/allergen) and at the 18-month exit visit. Basophil activation test (BAT) was performed with patient whole blood with the respective nut allergen extracts (0.01–1000 ng/mL; Flow CAST, BÜHLMANN, Switzerland). Molecular diagnosis for allergen specific IgG4 (sIgG4) and IgE (sIgE) was performed against 117 extracts and 178 molecular allergens utilizing the Allergy Explorer (MacroArray Diagnostics, Austria). Additionally, mass cytometry-based characterization of whole blood barcoded samples was performed to delineate the dynamics within the basophil compartment.

Results: Fourteen children achieved target maintenance dose and 18 month visit (3 withdrew and 1 did not reach target dose). The BAT showed a significant reduction in reactivity (%CD63+ basophils) to walnut ($p < 0.01$), pistachio ($p < 0.01$), cashew ($p < 0.01$), and peanut ($p < 0.01$) over time. Hazelnut BAT showed a similar trend in reduction. At 18-months, sIgE were significantly reduced and sIgG4 levels significantly increased in a treatment-specific manner. Mass cytometry revealed distinct changes in basophil subsets which reflect the process of desensitization at a single cell level.

Conclusion: Multi-nut VLOIT is accompanied by specific alterations of the basophil compartment and treatment-specific humoral changes reflective of the desensitization process.

Conflicts of interest: The authors did not specify any links of interest.

100187 | Effectiveness and safety of house dust mite-polymerized extract in pediatric patients with allergic rhinitis and/or asthma: A prospective cohort study

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*Presenting author: T. Garriga-Baraut

Background: Real-world evidence of subcutaneous house dust mites (HDM) allergoids in pediatric allergic patients is limited, particularly in children younger than five years of age. The objective of this study was to assess the effectiveness and safety of a glutaraldehyde modified extract of mites administered for one year under clinical routine conditions in children between 3 and 11 years old.

Method: In this multicenter, prospective, non-interventional study, children with HDM allergy received a subcutaneous immunotherapy (SCIT) of *Dermatophagoides farinae* (DF) and *Dermatophagoides pteronyssinus* (DPT) (1:1) (Probelte Pharma, Spain) according to a *rush* schedule and were monitored for 1 year. Patients were recruited from May 2019 until June 2021 after parents had signed informed consent. They had a positive prick test to DPT and/or DF and an allergen specific serum IgE level ≥3.5 KU/L. The primary endpoint was the number of adverse reactions according to the WAO SCIT grading system. Secondary endpoints included the Combined Symptoms and Medication Score (CSMS), as defined by EAACI, assessed for 1 month at baseline and approximately after 1, 6 and 12 months of SCIT. Additionally, the patient's perception of disease severity (Visual Analogue Scale, VAS) and the specific IgG_4 DPT and DF were measured. The study was approved by a clinical research Ethics Committee (Teknon Medical Center, Barcelona).

Results: 97 patients were enrolled in the study and 87 initiated SCIT. The mean age was 8.5 years (14.6% were between 3 and 5 years and 85.4% between 6 and 11 years). The diagnosis was rhinitis/rhinoconjunctivitis and asthma (77%) and rhinitis/rhinoconjunctivitis (23%). 15 adverse reactions in 1112 doses administered were reported (1.3%). 13 were local reactions in 8 patients (9.2%) and 2 were delayed reactions in 2 patients (2.3%). No patient withdrew treatment. After 12 months of immunotherapy, both CSMS and CSMS with only nasal symptoms decreased significatively ($p < 0.0001$) and IgG4 increased significatively ($p < 0.0001$). There was also improvement in the severity of symptoms and medication intake. No differences were found between asthmatic and no asthmatic patients.

Conclusion: Current data support that this HDM allergoid is effective and safe in children from 3 to 11 years old when administered under routine clinical conditions. ClinicalTrials.gov Identifier: NCT03963947.

Conflicts of interest: María Matas is employee at Probelte PharmaInmaculada Buendía is employee at Probelte Pharma.

100196 | Kinetics of peanut-specific sIgE and sigg4 during oral immunotherapy (OIT) and remission of allergy

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*Presenting author: P. Loke

Background: Oral immunotherapy (OIT) is effective at inducing desensitisation and leads to remission in a subset of patients. Remission is a preferred outcome as it allows treatment cessation, free allergen intake, and substantial improvement in quality-of-life. The key immune changes during OIT that support remission remain poorly characterised. Advances have been hampered by restricted access to effective remission treatments, longitudinal biosamples, and long-term challenge-confirmed outcomes.

Method: We examined longitudinal changes in peanut sIgE and sIgG4 in $n = 283$ children aged 1–10 years enrolled in three peanut OIT trials (PPOIT001, PPOIT002 and PPOIT003). Children received 18-months of peanut OIT (or placebo), and were followed for up to 66 months (4-years post-treatment). Plasma samples were obtained at pre-treatment ($n = 278$), end-of-treatment ($n = 241$), 1-year post treatment ($n = 160$) and 3–4 years post-treatment ($n = 47$). Remission was defined as passing a double-blind placebo-controlled food challenge (DBPCFC) at 4–8 weeks post-treatment. Children who received placebo provided a reference group. Linear models were used to compare log transformed immunoglobulin levels between groups at each time point. Mixed linear models were used to assess within group changes over time.

Results: High dose peanut OIT with or without probiotic resulted in significant reductions in peanut sIgE, with no differences between these groups, indicating modulation of the underlying peanut-specific allergic response with both approaches. Baseline sIgE and sIgG4 levels were significantly lower in children who achieved remission compared to those who did not; however the sIgG4:sIgE ratio at baseline was significant higher in children who achieved remission compared to those who did not, suggesting that the balance of Th2/blocking Igs is an important factor determining the likelihood of

remission. Importantly, peanut-sIgE levels in children with remission continued to reduce post-treatment, whereas levels in children who failed to achieve remission regressed towards baseline after treatment cessation

Conclusion: Remission following high dose OIT is associated with lasting and continued reductions in allergen-sIgE. Lower baseline sIgE and sIgG4, and higher baseline sIgG4/sIgE ratio, may increase the likelihood of achieving remission. Lasting reductions in peanut-sIgE amongst children with remission supports the validity of a 4–8 week elimination period prior to DBPCFC for assessing remission of allergy.

Conflicts of interest: MT reports having received consultant fees from Pfizer, Novartis and Prota Theraoeutics and has share options in Prota TherapeuticsPL reports having received consultant fees from SPRIM Consulting, and institutional grants from Siolta Therapeutics.

100261 | IGE reactivity in sera of patients with autoimmune diseases. A response using a synthetic multi-epitope protein constructed with t epitopes from *Ascaris lumbricoides* allergens

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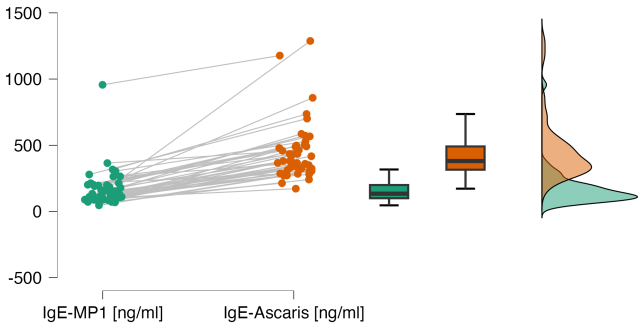
*Presenting author: E. Egea-Bermejo

Background: Helminth infections for *Ascaris lumbricoides* and exposure to mites allergens stimulate a Th2 immune response which is present in allergic diseases. Helminth proteins are known to modulate the host immune response and reduce the inflammatory response. We evaluate the IgE-reactivity to a molecule constructed from T-epitopes of *A. lumbricoides* and mites allergens (MP1) in sera from autoimmune patients.

Method: We designed and expressed MP1 from T-epitopes of *A. lumbricoides*, *D. pteronyssinus*, *D. farinae*, and *B. tropicalis* allergens, with a molecular weight of 20 kDa. By indirect ELISA, we evaluated IgE-reactivity to MP1 and to the whole-body extract of *Ascaris lumbricoides* in 45 sera from Colombian Caribbean patients with lupus nephritis (LN; $n = 25$), type 1 diabetes (T1D; $n = 10$) and Juvenil idiopathic arthritis (JIA; $n = 10$). Individuals with polyautoimmunity were excluded. All patients were referred to the study by their specialist doctor. A p-value <0.05 was considered statistically significant.

Results: We analyzed 45 sera from individuals with LN, T1D, or JIA. Ten males (22.2%) and 35 females (77.7%), of whom seven (15.5%) were children (6–11 years), 11 (24.4%) were adolescents (12–17 years), and 27 (60%) were adults (>18 years). IgE to whole-body extract of *A. lumbricoides* showed the following median concentrations: 484.2 ng/mL (RIQ: 203.4) in JIA patients, 325.6 ng/mL (RIQ: 179.3) in individual with LN, and 424.7 ng/mL (RIQ: 80.1) in T1D group; however, there was no statistically significant difference (K-W: 4.62; p-value: 0.099). On the other hand, IgE-reactivity to the multi-epitope protein (MP1) was 126.4 ng/mL (RIQ: 90.9) in JIA patients, 130.7 ng/mL (RIQ: 94.8) in individual with LN, and 148.8 ng/mL (RIQ: 102.1) in T1D group (data corresponding to the median); (K-W: 1.04; p-value: 0.593). Although no statistical differences were observed between patient groups, the IgE to MP1 in all patients (n: 45) (IgE median: 134.2 ng/mL; RIQ: 100) were significantly less compared to ascaris extract (IgE median: 380.7 ng/mL; RIQ: 175.8); (W: 0.732; p-value: 1.034×10^{-7}). Both measurements show a positive correlation (Rho: 0.638; p-value: 2.398×10^{-6}).

Conclusion: These preliminary results suggest that MP1 showed antigenic properties with low IgE-reactivity compared to *Ascaris lumbricoides* extract in individuals with autoimmune diseases. Further studies are needed to better understand the immune response induced by this molecule.



Conflicts of interest: The authors did not specify any links of interest.

100265 | The induction of IL-10 producing B regulatory cells leads to immunotolerance recovery with grass pollen subcutaneous immunotherapy

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*Presenting author: E. Palmer

Background: IL-10$^+$ regulatory B cells (Breg) play an essential role in the maintenance of tolerance to sensitised allergens in allergic rhinitis (AR) with and without asthma. We hypothesised that the frequency of IL-10$^+$ Breg cells is lower in seasonal and perennial AR and restored following allergen immunotherapy (AIT). Moreover, we hypothesise that IL-10$^+$ Breg cells may restore immune tolerance to the sensitising allergen through inhibition of allergen-specific Th2A cell responses.

Method: Peripheral blood mononuclear cells (PBMCs) were collected from non-atopic controls (NAC; $n = 18$), grass pollen allergic (GPA; $n = 18$), house dust mite allergic (HDMA; $n = 16$), cat allergic

(CA; $n = 16$) and GP-subcutaneous immunotherapy (GP-SCIT; $n = 16$) subjects. PBMCs were stimulated with CpG and CD40L for 72 hours and induction of IL-10$^+$ Breg cells were quantified by flow cytometry and unbiased clustering tools, viSNE and FlowSOM. IL-10 levels were measured using ELISA. Moreover, PBMCs were stimulated with anti-CD3/CD28 alongside recombinant IL-10 and neutralising IL-10 for 72 h and proliferation of Th2A cells were assessed by Cell Trace staining, quantified by flow cytometry.

Results: IL-10$^+$ Breg cell subsets were significantly induced in a time- and dose-dependent manner ($p < 0.01$; NAC and GPA). Significant dysregulation in the proportion of five IL-10$^+$ Breg cell subsets was observed in GPA ($p < 0.05$), HDMA ($p < 0.05$) and CA ($p < 0.05$) subjects. GP-SCIT subjects demonstrated increased IL-10$^+$ Breg cell frequencies compared to GPA individuals. Allergic individuals demonstrated decreased provision of IL-10 compared to NAC ($p < 0.01$; HDMA). IL-10$^+$ Breg cells were significantly increased in T cell immunoglobulin and mucin domain-1 (TIM-1) and IgG_4 expression compared to IL-10$^-$ Breg cells ($p < 0.05$). Unbiased machine learning tool FlowSOM revealed a specific IL-10$^+$ metacluster of dysregulated B cells found in both seasonal and perennial allergic patients compared to NAC ($p < 0.05$). Recombinant IL-10 modulated the proliferation of Th2A cells. This effect was neutralised by anti-IL-10.

Conclusion: IL-10$^+$ Breg cells are dysregulated during allergic inflammation, with similar Breg cell subset aberrations underlying both perennial and seasonal allergies. Moreover, GP-SCIT restores the frequency of IL-10$^+$ Breg cell frequencies.

Conflicts of interest: The authors did not specify any links of interest.

100401 | Oral immunotherapy in alpha-gal red meat allergy: Could specific IGE be a potential biomarker in monitoring management?

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*Presenting author: D. Eyice Karabacak

Background: Early intervention with oral immunotherapy (OIT) is a promising treatment for food allergies. Our aim was to establish the long-term safety and efficacy of a novel red meat OIT in galactose-alpha-1,3-galactose (alpha-gal) allergy in adults.

Method: Out of 20 patients with red meat allergy confirmed by placebo-controlled food challenge test five (41.66%) underwent an early red meat OIT, seven (58.33%) underwent a delayed protocol and eight patients who were not desensitized formed the patient control group. 15 and 27 day red meat OIT for early-onset and delayed-onset alpha-gal allergy were administered, respectively. Desensitized patients were recommended to continue eating at least 100 g red meat every day for 6 months and every other day in the following 6 months. After a year, the consumption was recommended 2/3 times in a week. Patients were followed-up with skin tests with commercial beef and lamb extracts, fresh raw/cooked beef and lamb and cetuximab and also with serum alpha-gal specific Immunoglobulin-E (sIgE) in the first and fifth years. Additionally, patients who were not desensitized formed the patient control group.

Results: 12 out of 20 alpha-gal red meat allergic patients underwent OIT and all patients became tolerant to red meat. During OIT, only two patients experienced urticaria or anaphylaxis. Following the first year of OIT, patient 12 did not eat meat regularly and even had to take a break for 14 days during his military service. That's why he is dropped out from the study. Besides, patient 7 and patient 10, after tick bites at the 12th and second months of desensitization respectively became intolerant to red meat. During the five year follow-up, nine patients uneventfully consumed red meat. The median alpha-gal sIgE level gradually decreased in the follow-up in the OIT group while remained unchanged in the control group ($p = 0.016$). In two patients, rare tick bites acted as inducers of hypersensitivity reactions with concomitant elevation of alpha-gal sIgE levels whereas in one patient with low follow-up alpha-gal sIgE levels experienced uneventful frequent tick bites.

Conclusion: Our study showed the long-term safety and efficacy of alpha-gal OIT. Additionally, alpha-gal sIgE seems to be a potential biomarker to monitor OIT.

Table 4: 15 day oral immunotheraphy protocol for early alpha-gal allergy

Solution 1: 0.1% Cooked Meat Extract*					
Day	First dose(0.min)	Second dose(30.min)	Third dose(60.min)	Fourth dose(90.min)	Daily Cumulative dose (mg)
Day 1	10 drops	10 drops	20 drops	40 drops	80 drops
Solution 2 : 1 % Cooked Meat Extract**					
Day 2	5cc	5 cc	10cc	20cc	40cc
Cooked meat***					
Day 3	2 mg	2mg	4mg	8mg	16mg
Day 4	4mg	4mg	8mg	16mg	32mg
Day 5	8mg	8mg	16mg	32mg	64mg
Day 6	16mg	16mg	32mg	64mg	128mg
Day 7	32mg	32mg	64mg	128mg	256mg
Day 8	64mg	64mg	128mg	256mg	512mg
Day 9	128mg	128mg	256mg	512mg	1g
Day 10	256mg	256mg	512mg	1g	2g
Day 11	512mg	512 mg	1 g	2g	4g
Day 12	1 g	1g	2g	4g	8 g
Day13	2 g	2g	4 g	8g	16g
Day 14	4 g	4g	8g	16g	32g
Day 15	8 g	8g	16g	32g	64g

* **Solution 1**: 10 mL solution 2 in 90 mL water (0.1%). 1 mL: 20 drops

** **Solution 2**: 6 mg meat cooked in 600 mL water (1%). 1mL: 20 drops

*****Cooked meat**

*In this protocol, we started with increasing amounts of diluted broth on the first two days.

On the third day, 1 mg of cooked meat was started and a total of 16 mg was given.

The doses were doubled daily until the amount of 100 g/day was reached.

*Each dose was given in four separate courses 30 min apart.

Conflicts of interest: The authors did not specify any links of interest.

100414 | Immunotherapy and biologics in the management of IGE-mediated food allergy: Systematic review and meta-analyses of efficacy and safety

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Background: Food allergy (FA) is a potentially life-threatening chronic condition that is becoming an increasing public health problem worldwide. This systematic review (SR) was carried out in inform the development of clinical recommendations on the treatment of IgE-mediated FA with biologics and/or IT for the update of the EAACI guidelines.

Method: A SR of randomized-controlled trials or quasi-controlled trials was carried out. Studies were identified via comprehensive search strategies in Medline, Embase, and Cochrane Library, up to April 2022. **Population:** Human adults, children, and adolescents with IgE-mediated FA. **Intervention:** IT and/or biologics. **Comparator:** Placebo or standard-of-care (allergen avoidance). **Outcome:** Efficacy (desensitization, sustained unresponsiveness (SU), long-term tolerance), quality of life, and safety (systemic and local adverse reactions (AR)). The Cochrane RoB tool was used to assess the risk of bias. It was reported according to PRISMA and registered in PROSPERO CRD4202229828.

Results: After screening, 121 studies were included (111 for IT and 10 for biologics). Few studies had a low risk of bias and most studies showed high heterogeneity in designs and results. Metanalysis showed a positive effect of biologics and IT in terms of relative risk (RR) for achieving tolerance to the culprit food compared to avoidance or placebo. Omalizumab for any FA showed a RR of 2.17 [95% confidence interval: 1.22, 3.85]. For peanut allergy, oral IT (OIT) had a RR of 11.94 [1.76, 80.84] vs avoidance or placebo, sublingual IT (SLIT) had a RR of 3.00 [1.04, 8.66], and epicutaneous IT (EPIT) of 2.16 [1.56, 3.00]. OIT had a RR of 5.88 [2.27, 15.18] for cow's milk allergy, and of 3.43 [2.24, 5.27] for egg allergy. There was not enough data on SLIT or EPIT for this allergens. Most ARs reported where mild, for OIT the most common was gastrointestinal and for EPIT skin symptoms. There was reduced data on severe or life-threatening ARs. There was limited evidence for long term efficacy and quality of life.

Conclusion: Biologics and IT, alone or in combination, are effective and safe in the management of IgE-mediated FA, although the evidence is not of high quality. Better standardization of desensitization protocols and outcome measures is key to support the use of IT and biologics more widely.

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100517 | Oral immunotherapy for cashew nut and peanut allergy in children 2018–2022 – A retrospective single-center study

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Background: Oral immunotherapy (OIT) in children has been increasingly used in recent years. While there is evidence of efficacy for OIT in peanut (PN) allergy, there is limited data on OIT in cashew nut (CN) allergy. The aim of this study was to investigate the safety and feasibility of CN OIT and to compare it with PN OIT. We also assessed the factors that influence side effects and the success of the therapy.

Method: This retrospective analysis included children who had undergone OIT with CN (n = 24) or PN (n = 38) between 2018 and 2022 at the University Children's hospital Basel. Standard oral food challenge (OFC) to determine the individual reactive dose was performed in all CN and 25 PN allergic patients, while OIT was started with a dose escalation regimen up to 6.4 mg nut protein in 13 severe PN allergic patients. Side effects during the oral food challenge and therapy were graded using the oFASS-5 scale. Patients were instructed to eat a daily nut dose that was gradually increased by approximately 20%–30% every two weeks up to a maintenance dose of 1 gram of nut protein. After 18–24 months of consuming the maintenance dose, a second oral food challenge tested for a tolerance of 4.4 grams of protein.

Results: Median patient age was 7 years (range 2–17), and the mean reactive dose was 576 mg of CN protein and 441 mg of PN protein. During the updosing, only 4 (16%) CN allergic patients showed mild to moderate side effects, while 21 (55%) of those with PN OIT had side effects including 5 of them with severe reactions (all with high initial specific IgE levels). Three patients with PN OIT discontinued

therapy due to side effects, none in the CN OIT group. Of the total study population, 16 CN and 27 PN patients haved reached the maintenance phase or completed the therapy with tolerance in the second OFC. The mean duration to reach the maintenance phase was 265 days for CN OIT and 327 days for PN OIT. Children with older age, asthma diagnosis, or another food allergy took longer to reach the maintenance phase.

Conclusion: Our study shows that OIT for CN and PN allergy in children is generally well tolerated. Notably, CN OIT was associated with only mild side effects, indicating that OIT is a valuable approach for treating CN allergy. However, certain patient characteristics such as older age, asthma diagnosis, and high initial specific IgE levels were associated with a higher risk of side effects and longer treatment duration. Therefore, considering these factors during OIT planning can optimize treatment outcomes and further improve the safety profile of this promising therapy.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on allergen immunotherapy II

000932 | Non-interventional studies with the SQ grass, tree, ragweed, and house dust mite slit-tablets – a systematic literature review

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Background: In randomised controlled trials (RCTs), allergy immunotherapy (AIT) administered as SQ sublingual immunotherapy (SLIT)-tablets has shown to be an effective and well-tolerated treatment of allergic rhinitis due to grass, tree, ragweed, and house dust mite (HDM). Non-interventional studies (NISs) are conducted to further investigate effectiveness, safety, tolerability, adherence, and/or other aspects of authorised medicinal products in real-world clinical settings. This systematic literature review presents an overview of the totality of evidence from NISs with the SQ grass, tree, ragweed, and HDM SLIT-tablet.

Method: Methods: PubMed, ClinicalTrials.gov, and EU Clinical Trials Register were screened for NISs with SQ grass, tree, ragweed, and HDM SLIT-tablets in June 2022 using the string ("Product Surveillance, Postmarketing" [MH] OR "post-marketing" OR "post-authorization" OR "cohort" or "case-control" OR "observational" OR "non-interventional" OR prospective OR "real-world" OR retrospective OR "drug utilization" OR longitudinal) AND (grazax OR itulazax OR ragwizax OR acarizax OR grastek OR itulatek OR ragwitek OR miticure OR odactra OR ALK[AD] OR ALK-abello[AD]) AND ("2006/01/01" [PDAT]: "2022/06/15"[PDAT]). Non-English, phase I-III trials, and publications prior to 2006 were excluded together with publications based on secondary data as well as cases, where it was unclear, if SQ SLIT-tablets were studied.

Results: Of almost 150 screened publications, 21 publications based on 20 individual NISs with SQ grass, ragweed, and HDM SLIT-tablets were included (Table 1). The total study population consisted of 13,172 subjects (8501 [65%] adults, 2987 (23%) children, and 1684 [13%] not specified). The publications included data from Europe (16 (76%]), North America (2 [10%]), and Asia (3 [14%]), and had clinical effectiveness (2 [10%]), quality of life/patient satisfaction (4 [19%]), safety/tolerability (12 [57%]), adherence (1 [5%]), or other (2 [10%]) as primary objective. Generally, the SQ SLIT-tablets improved symptoms and were well-tolerated. No NISs with the SQ tree SLIT-tablet were identified, likely explained by the treatment only being recently marketed.

Conclusion: The totality of real-world clinical evidence from NISs with the SQ grass, ragweed, and HDM SLIT-tablets is substantial and further complements the efficacy and safety profile established in RCTs. NISs studying clinical efficacy and safety of the SQ tree SLIT-tablet is warranted.

	Total	SQ SLIT-tablet studied*		
		Grass	Ragweed	HDM
NISs, n (%)†	20 (100)	14 (70)	2 (10)	7 (35)
Publications, n (%)†	21 (100)	15 (71)	2 (10)	7 (33)
Study population				
Total, n (%)†	13,172 (100)	7,818 (59)	1,491 (11)	6,743 (51)
Adults,‡ n (%)†	8,501 (100)	4,394 (52)	826 (10)	4,831 (57)
Children,‡ n (%)†	2,987 (100)	1,740 (58)	665 (22)	1,912 (64)
Not specified, n (%)	1,684 (100)	1,684 (100)	0 (0)	0 (0)
Region§				
Europe, n (%)	16 (100)	13 (81)	0 (0)	3 (19)
North America, n (%)†	2 (100)	2 (100)	2 (100)	1 (50)
Asia, n (%)	3 (100)	0 (0)	0 (0)	3 (100)
Primary objective§				
Clinical effectiveness, n (%)	2 (100)	1 (50)	0 (0)	1 (50)
QoL/patient satisfaction, n (%)†	4 (100)	3 (75)	1 (25)	2 (50)
Safety/tolerability, n (%)	12 (100)	8 (67)	1 (8)	4 (33)
Adherence, n (%)†	1 (100)	1 (100)	0 (0)	0 (0)
Other, n (%)	2 (100)	2 (100)	0 (0)	0 (0)

HDM, house dust mite; n, number; NISs, non-investigational studies; SLIT, sublingual immunotherapy, QoL, quality of life
* The SQ tree SLIT-tablet is not shown in the table, because no NISs studying the SQ tree SLIT-tablet was included in the final analysis
† The product-specific percentages >100%, because two NISs studied >1 SQ SLIT-tablet
‡ Age group as defined by authors
§ Presented n represents number of publications

Table 1. Overview of number of included NISs, publications, study subjects, regions, and primary objectives in total and by the studied SQ SLIT-tablet.

Conflicts of interest: CJ has received payment for educational activities from ALK-Abelló. JMCSS has no conflicts of interests to declare. AH has previously participated as investigator in clinical trials sponsored by ALK-Abelló, has received remuneration from ALK-Abelló for educational presentations, and is advisory board member for ALK-Abelló.

001220 | House dust mite sublingual allergen immunotherapy tablet is safe and well tolerated in Dutch daily practice

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Background: 49% of clinically diagnosed allergic rhinitis (AR) patients are sensitized to house dust mite (HDM). If allergen avoidance and symptomatic medication fail, allergen immunotherapy may be indicated. We investigated safety, tolerability, and compliance of HDM-sublingual immunotherapy tablets (HDM-SLIT) in adults in daily practice in the Netherlands.

Method: In the RELIEF study, 2017–2020, daily intake of 12 SQ-HDM SLIT-tablet was investigated in a prospective, multi-centre, observational study with 4 study visits during 1-year follow-up. Safety, tolerability, symptomatic and other relevant concomitant medication, compliance, Control of Allergic Rhinitis and Asthma Test (CARAT) questionnaire, and treatment satisfaction data were collected. MCID of CARAT is 4 points. Data were presented descriptively, except for changes over time where longitudinal regression analysis was applied.

Results: 415 adult patients, mean age 36.6 years, 61.4% female, with on average an 8-year long AR history, were included. 36% were asthmatic and 79% were polysensitised.

Possibly-related adverse events (AEs) were reported by 65.3% and mostly mild (67%): AEs included oral allergic reactions (58.6%), respiratory (12.4%) and gastrointestinal symptoms (9.4%). All AEs were non-serious except one case of angioedema. The patient fully recovered. The percentage of patients reporting AEs decreased from 51.8% at day 1 to 5.8% after 1 year in those remaining on treatment. During the initial year of treatment, 60 (14.5%) patients stopped due to AEs and 76 (18.3%) due to motivational/other reasons. A compliance rate ≥80% was achieved in 86.6% of patients at 1 year.

CARAT scores increased significantly and clinically relevant by 6.3 points after 1 year. Symptomatic medication use decreased (96.1% to 77.4%). Most patients (62.4%) and investigators (69.4%) were satisfied or very satisfied with the HDM-SLIT treatment.

Conclusion: HDM-SLIT is a safe and well-tolerated HDM-AR treatment. AEs occur often but are mostly mild and decreasing significantly during the first year. CARAT scores improved and symptomatic medication use decreased suggesting better control of AR with HDM-SLIT treatment in daily practice. When patients continue therapy, compliance is high and satisfaction is good. However, 14.5% and 18.3% of patients stopped due to AEs or motivational reasons, respectively. Patient follow-up and compliance remain important points of attention when starting HDM-SLIT.

Conflicts of interest: LPvdZ & EU are employees of the sponsor of the study ALK-Abello BV; ZTP, MCA, ANvdM and ACK received fees from ALK-Abello BV.

000116 | *Juniperus oxycedrus* pollen allergoid immunization in mice induces humoral and cellular immune responses against natural group 1 allergens from several Cupressacea species

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Background: Seasonal respiratory allergy induced by the inhalation of the pollen from several species of the Cupressaceae family is common. Cypress allergic individuals may show co-sensitization to several species from the Cupressaceae family. *Juniperus oxycedrus*, a species belonging to the Cupressaceae family grows abundantly in many geographical areas. Allergen-specific immunotherapy remains the only available causative treatment for patients with allergic diseases. Allergoids are produced by chemically modifying native allergen extracts. Allergoids retain the ability of the allergen to elicit an immunologic response while decreasing the risk of anaphylaxis. Objective: To study whether immunization of mice with J. oxycedrus pollen allergoids, polymerized with glutaraldehyde generate an immune response against group 1 allergens from Cupressaceae species.

Method: BALB/c mice were immunized with *J. oxycedrus* native pollen extracts, or allergoids. Allergen-specific antibodies were studied by ELISA and Western blot using the sera of immunized and control mice. Splenocyte specific-proliferation was performed by Flow Cytometry; cytokine production was quantified by ELISA. Extracts from J. oxycedrus and *Cupressus arizonica* pollen were prepared by extraction in PBS. Purification of natural group 1 allergen from the extract was performed by precipitation with ammonium sulfate followed by affinity chromatography using a Concanavalin A column

Results: Intraperitoneal immunization of mice with *J. oxycedrus* pollen allergoids induced a stronger humoral response than the native counterpart with high titers of total IgG, IgG1 and IgG2a specific to group 1 allergens from the analysed Cupressaceae species. A higher IgG2a/IgE ratio was observed with *J. oxycedrus* allergoid. Sera from immunized mice with allergoids reacted with the 40–42 KDa bands which corresponds to group 1 allergen from several Cupressacea species by Western blot. Specific proliferative responses were also observed in spleen cells assayed in vitro from mice immunized with *J. oxycedrus* allergoids.

Conclusion: *Juniperus oxycedrus* pollen allergoids administered in mice promote the generation of humoral and cellular responses in a greater extent than native allergens against group 1 allergen from Cupressaceae species.

Conflicts of interest: The authors did not specify any links of interest.

001078 | Prevalence of cypress pollen sensitization and its clinical relevance in the north of Portugal

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Background: Cypress pollen is becoming an increasing cause of respiratory allergy. In the last 10 years, there has been in Portugal an increase in its prevalence, namely in the northern region (Caeiro et al, 2020 RPIA). However, the clinical impact of this exposure is unknown. We aimed to analyze the prevalence of sensitization in a cohort of patients evaluated at an Allergy and Clinical Immunology department in Porto, in the north of Portugal.

Method: We randomly selected a cohort of 229 patients (59.4% females; 1–73 years old) who were sensitized to at least 1 of the most common aeroallergens tested between 2020 and 2022. The commercial extracts used in SPT were provided by Roxall Aristegui and included *D. pteronyssinus*, *D. farinae*, *L. destructor*, grass mix, weed mix, plane, birch, olive, *Parietaria*, *A. alternata*, *C. herbarum*, *A. fumigatus*, dog and cat dander. The concentration (grains/m^3) of atmospheric cypress pollen was quantified using a hirst-type spore trap, in the same period.

Results: The atmospheric concentration of cypress pollen (median, [IQR]) was significantly higher from mid-January to late March 2021 (2.9 [4.9]), compared to the same period in 2020 (9.7 [39.8]) and 2022 (7.8 [15.5]), $p < 0.001$.

Cypress pollen sensitization was identified in most patients (n = 152; 55.7%), with only 1 monosensitized. Most cases had allergic rhinitis (142, 93.4%), 72 (47.4%) with allergic conjunctivitis, and 59 (38.8%) asthma. Symptoms were perennial in 113 (74.3%) patients and only during spring in 84 (55.3%). Cosensitization with house dust mites was found in 140 (92.1%) patients, whereas for grasses in 120 (85.5%), weeds in 65 (42.3%), and other tree pollens in 42 (27.6%). Two patients were under allergen immunotherapy with cypress extract.

Conclusion: Cypress pollination in our region occurs from January to the end of March. In this cohort most of the patients sensitized to cypress were polysensitized, namely to allergens that are associated with perennial symptoms. Therefore, further studies are needed to ascertain the clinical impact of cypress sensitization, such as allergen challenges, as well as possible implications of increased exposure to cypress pollen.

Conflicts of interest: The authors did not specify any links of interest.

001580 | Sensitization to Cupressaceae in Portugal – A multicentric study

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Background: Pollens from the Cupressaceae family are common allergens in the Mediterranean area; however, its real prevalence and its clinical relevance in patients with respiratory allergy is not precisely established.

Aim: To characterise the clinical and molecular profile in a subgroup of allergic rhinitis patients with positive skin tests (SPT) o Cypress and Cup a 1.

Method: Seasonal allergic rhinitis (AR) patients (≥11 years-old) from 7 allergy centres in Portugal without previous allergen immunotherapy (AIT), and positive SPT to both Cypress and Cup a 1 (Diater®) were included. Total IgE and specific IgE (sIgE) were determined using ALEX^2 (MacroArrayDX, Wien, Austria). For sIgE to Cup s, Cup a1, Cry j1, Pru p3, Pru p7 values ≥0.3 kUA/L were considered positive. Descriptive statistics were calculated using frequencies, percentages, means and interquartile range (IQR). Comparisons of sIgE to Cup a 1 level according to the severity of rhinitis, diagnosis of asthma or conjunctivitis were tested using ANOVA and T-Test accordingly.

Results: We included 48 patients from 7 centres (North = 3/Centre = 16/South = 29) of Portugal (52% females, 88% adults, mean age 36.2 ± 17.3 years (min 11; max 71)). All had rhinitis (69% persistent moderate-to-severe), 58% had asthma and 60% conjunctivitis. Considering ALEX^2 results, 18.8% (n = 9) were sensitised to cypress without sensitisation to other pollens. Total IgE median value [IQR] was 109 [303.2] kUA/L. Regarding the sIgE (media [IQR] – kUA/L) determined: 6 patients were sensitised to Cup s (0.6 [0.2]), 41 to Cup a1 (8 [17.5]), 26 to Cry j1 (1.4 [4.6]), 3 to Pru p3 (4.4 [8.8]) and none to Pru p7. We found a high frequency of sensitization to Cup a 1 without sensitization to Cup s (Table 1). We did not find a significant

variation in sIgE to Cup a1 levels according to rhinitis severity (p = 0.5), the presence of asthma (p = 0.6) or of conjunctivitis (p = 0.3). The screening of patient's sera by Immunoblotting revealed a sIgE binding to a protein with a molecular weight compatible with Cup a1 in most the patients.

Conclusion: In Portugal, sensitisation to Cypress is more common in the context of sensitisation to other pollens and is associated with a high frequency of rhino conjunctivitis. Cup a1 was the allergen identified in most Cypress allergic patients. These data highlight the importance of Cup a1 in the diagnosis and, consequently, in the selection of this same molecular allergen in the composition of the ITA in cypress allergy.

Table 1 – Cypress sensitisation profile of the studied population

		sIgE to Cup a 1 (n)	
		< 0.3 kUA/L	>0.30 kUA/L
sIgE to Cup s (n)	< 0.3 kUA/L	7	35
	> 0.30 kUA/L	0	6
		sIgE to Cry j1 (n)	
		< 0.3 kUA/L	>0.30 kUA/L
sIgE to Cup s (n)	< 0.3 kUA/L	18	24
	>0.30 kUA/L	4	2
		sIgE to Cup a1 (n)	
		< 0.3 kUA/L	>0.30 kUA/L
sIgE to Cup s + sIgE to Cry j1 (n)	< 0.3 kUA/L	3	15
	>0.30 kUA/L	0	2

Conflicts of interest: The authors did not specify any links of interest.

000034 | Sublingual immunotherapy with dust mite tablet was successfully introduced and effective in preschoolers with allergic rhinitis: A pilot study

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Background: In Japan, house dust mite (HDM) sublingual immunotherapy (SLIT)-tablet is not age-restricted for the treatment of allergic rhinitis (AR), however, the evidence in pre-school children is limited. This study aimed to investigate the efficacy and safety of HDM SLIT-tablet in preschool children.

Method: The study was a single-center, controlled, open-label, prospective clinical trial. Children (1–4 years) with AR were divided into a SLIT group (n = 22) and a control group (n = 13) according to their guardians' preferences. In the SLIT group, HDM SLIT-tablet were administered once-daily by the guardians at a daily dose of 3300 JAU during the first week followed by a daily dose of 10,000 JAU (6 SQ-HDM) for a total of 12 months. Use of symptomatic treatment was allowed when AR was uncontrolled. The control group received symptomatic treatment only. AR symptom score, AR medication score, and wheezing frequency were assessed monthly. Immunological changes were assessed every 6 months. Adverse reactions were recorded daily in the SLIT group.

Results: At baseline, median age was 41 and 34 months and AR symptom score was 4 and 4 (p = 0.15 and p = 0.33) in the SLIT and control group, respectively. In the SLIT group, the AR symptom score at 12 months (3) significantly decreased compared to baseline (p < 0.01), and significantly decreased compared to the control group at 12 months (6) (p = 0.01). AR medication score significantly decreased at 12 months compared to baseline (p = 0.03). In the control group, no statistically significant changes from baseline to 12 months were seen for AR symptom or medication scores. The frequency of wheezing developed during the study was 0.3% (25 episodes) and 0.7% (27 episodes) in the SLIT and control groups, respectively (p < 0.01). Adverse reactions related to SLIT were all mild and occurred in 8 patients (36%). In the SLIT group, *Dermatophagoides farinae* (*D. farinae*)-specific IgE (sIgE) significantly increased at 6 months (p < 0.01) from baseline but had returned to baseline-level at 12 months. In the control group, sIgE significantly increased at 12 months compared to baseline (p = 0.01). *D. farinae*-sIgG$_4$ and HDM IgE blocking factor significantly increased at 12 months from baseline (p < 0.01) in the SLIT group. No changes were seen in the control group.

Conclusion: This pilot study showed that SLIT with HDM SLIT-tablet for AR in children aged 1–4 years could be performed effectively and safely and induced HDM-specific immunological changes.

Conflicts of interest: K Doi is an employee of Torii Pharmaceuticals, Inc.

001381 | The clinical usefulness of spit-out method in house dust mite sublingual immunotherapy

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Background: Sublingual immunotherapy (SLIT) is an effective treatment for allergic rhinitis. SLIT is usually administered by the swallow method which involves keeping hold it under the tongue for 1 minute and swallowing it. However, there are some patients who have difficulty continuing it because of its adverse reactions (ARs). We evaluated the effectiveness of the spit-out method in SLIT which involves spitting out the medication after holding it in the mouth. This aids in the reduction of ARs associated with SLIT.

Method: We retrospectively analyzed the data of children who started house dust mite (HDM) SLIT for perennial allergic rhinitis at our facility between January 2017 and September 2020. We included the patients who changed to the spit-out method due to ARs. After the ARs had improved, we instructed the patients to return to the swallow method. The rate of patients who returned to the swallow method and continued SLIT was estimated using the Kaplan–Meier method. Failure was defined as discontinuation of SLIT or

requirement of further changes in the oral method because their ARs did not reduce.

Results: Among 238 patients who started HDM SLIT, 151 patients (64%) had ARs. We analyzed 28 patients who changed to the spit-out method excluding those with missing data. The median age was 9.7 years. Altogether, 57% of the individuals were male. The rates of complications; seasonal allergic rhinitis, allergic conjunctivitis, bronchial asthma, atopic dermatitis and food allergy were 86%, 57%, 36%, 32% and 43%, respectively. Their median level of D. pteronyssinus-specific immunoglobulin E was 96.1 U_A/mL. Their median total nasal symptom-medication score was 20.0. Oral/pharynx, skin/mucosal, digestive (other than oral/pharynx), and respiratory adverse reactions were observed in 86%, 50%, 25%, and 11% of them, respectively. With the introduction of the spit-out method, the symptoms in 71%, 42%, 86%, and 100% of them were resolved, respectively. The estimated rate of returning to the swallow method and continuing SLIT was 67% at 2 years after changing to the spit-out method.

Conclusion: About two-thirds of the patients who started the spit-out method showed a reduction in ARs and returned to the swallow method. The spit-out method may be useful for patients who have difficulty continuing the swallow method due to ARs associated with HDM SLIT.

Conflicts of interest: The authors did not specify any links of interest.

000512 | The SQ slit-tablets significantly improve quality of life with consistent improvements across ocular and nasal dimensions in adults with grass, tree, ragweed and house dust mite allergic rhinitis (AR)

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Background: Ocular and nasal symptoms caused by allergic rhinoconjunctivitis (ARC) can negatively impact many aspects of quality of life (QoL). The efficacy and safety of allergy immunotherapy, when administered as SQ sublingual immunotherapy (SLIT)-tablets, have been confirmed across large randomised, double-blind, placebo-controlled trials in adults with grass, tree, ragweed, and house dust mite (HDM) ARC. This pooled analysis investigates whether the reduction in symptom burden found across the clinical trials is supported by improvements in QoL.

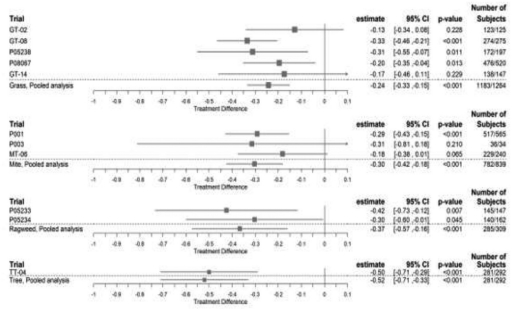
Method: Data from 11 phase II/III randomised placebo-controlled trials across the SQ grass, tree, ragweed and HDM SLIT-tablets (Grass: *N* = 2447; Tree: *N* = 573; Ragweed: *N* = 594; HDM: *N* = 1621) were included. QoL was assessed using the standardised Rhinitis Quality of Life Questionnaire (RQLQ) with the exception of three grass trials (GT-02, GT-08, GT-14) that used the non-standardised version. The overall RQLQ scores were expressed as a mean of seven dimensions, with two of the dimensions being related to ocular and nasal symptoms, respectively. In the pooled analysis, treatment was used as a fixed effect, the trial, and the interaction between region/country with the trial were used as random effects. Individual trials were analysed as pre-defined in the protocols and using the approved doses in Europe and North America.

Results: The pooled analysis showed consistent and statistical significant improvements in overall RQLQ scores across all four SQ SLIT-tablets vs. placebo (Pooled estimate [95%CI], p value. Grass: −0.20 [−0.28, −0.12], $p < 0.001$. Tree: −0.42 [−0.58, −0.26], $p < 0.001$. Ragweed: −0.36 [−0.55, −0.17], $p < 0.001$. HDM: −0.28 [−0.39, −0.17], $p < 0.001$). Across the two dimensions related to ocular and nasal symptoms, the pooled analyses demonstrated significant improvements vs. placebo for all four SQ SLIT-tablets (SQ SLIT-tablet vs. placebo [Ocular; Nasal]: Grass: $p < 0.001$; $p < 0.001$. Tree: $p < 0.001$; $p < 0.001$. Ragweed: $p < 0.001$; $p = 0.002$. HDM: $p < 0.001$; $p < 0.001$). All point estimates from individual trials favored active treatment and effect sizes of the pooled analyses were between −0.24 to −0.52 and −0.28 to −0.40 for the ocular and nasal dimensions, respectively (Figure).

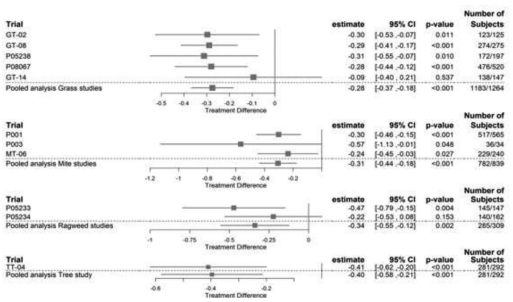
Conclusion: The proven efficacy of SQ SLIT-tablets to reduce symptoms across four of the most common respiratory allergens, is further supported by concurrent significant improvements in both the ocular and nasal QoL dimensions from the RQLQ questionnaire.

Figure: Estimated treatment difference (SQ SLIT-tablets vs. placebo) in the ocular and nasal dimension scores assessed by the Rhinitis Quality of Life Questionnaire (RQLQ)

A: RQLQ ocular symptoms dimension:



B: RQLQ nasal symptoms dimension:



Conflicts of interest: GR was an investigator in the ALK Abelló Grazax Asthma Prevention (GAP) trial, is a consultant/speaker for ALK Abelló, and a consultant for AstraZeneca. GR has received speaker honoraria from ALK-Abello, Allergen Therapeutics, Meda and funding for asthma studies from that National Institute for Health and Care Research (NIHR), National Institutes of Health (NIH), the EU, and the Medical Research Council (MRC). SRD has received grant support from Immune Tolerance network, National Institute of Allergy and Infectious Diseases, NIH, USA and personal fees for consultancies from ALK, Allergopharma, Angany, Revelo and lecture fees from Abbott Laboratories, ALK, Conveners events LLC, Pneumo Update GmbH, Seqirus and Stallergenes. MB has received consulting fees from ALK-Abelló, Merck, Stallergenes Greer, Sanofi/Regeneron as a consultant and speaker, Lanier Biotherapeutics as consultant, AstraZeneca as consultant, and Ready, Set, Food as consultant, speaker/writing fees from ALK-Abelló and Merck, and has participated on a Data Safety Monitoring Board/Advisory Board for ALK-Abelló and Merck. KFA, HN, TS are employees of ALK. DB has received grant support from Aimmune, ALK, Amgen, AstraZeneca, Adare, Bellus, Cheisi, Genentech, GlaxoSmithKline, IQVIA, Leo, Novartis, Novum, Regeneron, Sanofi, Suzhou, and TEVA and served as an advisor for ALK America, Gerson-Lehman, GSK, Guidepoint Global and Regeneron.

000868 | Pollen sensitization profiles in a cohort of German allergic patients

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Background: Pollen is one of the main causes of allergic symptoms. Furthermore, most of patients are sensitized to more than one pollen. Therefore, a better knowledge of the allergenic sensitization profile of patients in real life is needed and could be helpful for optimized and personalized allergen immunotherapies. The aim of this study was to evaluate the rate of polysensitization to pollen allergens in a German cohort.

Method: Five hundred allergic patients from different regions of Germany were included in the study. The diagnosis of allergy was based on case history, clinical allergic signs (allergic rhinitis and/or bronchial asthma) and data of skin prick-tests to aeroallergens. Sera samples were collected and analyzed by ImmunoCAP™ to determine the specific IgE levels to 16 main allergenic sources. After this analysis and depending on the results obtained, sIgE to 17 related allergenic sources was determined.

Results: Out of the 500 subjects included in the study, 382 (76%) were sensitized to any of the pollens studied. From these patients, 291 (76%) were sensitized to grasses (*Phleum pratense*), 307 (80%) to trees (*Betula alba*, *Olea europaea*, *Cupressus arizonica* and *Platanus acerifolia*) and 130 (34%) to weeds (*Salsola kali*, *Plantago lanceolata*, *Parietaria judaica* and *Artemisia vulgaris*).From the 382 patients sensitized to pollen allergens, 61 (16%) were monosensitized to grasses, 70 (18.3%) to trees and 11 (2.9%) to weeds. A total of 121 patients (31.7%) were polysensitized to grasses and trees, 106 (27.7%) to grasses, trees and weeds, 10 (2.6%) to trees and weeds and 3 (0.8%) to grasses and weeds. The most relevant pollen allergens were *Phleum* and *Betula*. A total of 291 patients (58.2%) were sensitized to *Phleum* and 295 (59%) to *Betula*. The great majority, 218 (75%) patients, were polysensitized to both allergens and only 2.4% were monosensitized to *Phleum* and 11% to *Betula*. Furthermore, 90% of the *Phleum* sensitized patients showed also polysensitization to other grass allergens (*Festuca*, *Lolium* and *Dactilys*). From the patients sensitized to *Betula*, 70% showed also polysensitization to *Quercus* and 80% to *Fagus*.

Conclusion: Most of the patients were polysensitized to a wide range of grass, *Betula* and weeds pollen combinations. These results confirm the importance of the polysensitization studies in allergic patients to improve the allergic diagnosis and offer them personalized immunotherapy treatments.

Conflicts of interest: Prof. Dr. Mösges reports grants and personal fees from LETI, during the conduct of the study; personal fees from ALK, grants from ASIT biotech, personal fees from allergopharma, personal fees from Allergy Therapeutics, grants and personal fees from Bencard, grants, personal fees and non-financial support from Lofarma, non-financial support from Roxall, grants and personal fees from Stallergenes, grants from Optima, personal fees from Friulchem, personal fees from Hexal, personal fees from Servier, personal fees from Klosterfrau, non-financial support from Atmos, personal fees from Bayer, non-financial support from Bionorica, personal fees from FAES, personal fees from GSK, personal fees from MSD, personal fees from Johnson&Johnson, personal fees from Meda, personal fees and nonfinancial support from Novartis, non-financial support from Otonomy, personal fees from Stada, personal fees from UCB, non-financial support from Ferrero, grants from BitopAG, grants from Hulka, personal fees from Nuvo, grants and personal fees from Ursapharm, personal fees from Menarini, personal fees from Mundipharma, personal fees from Pohl-Boskamp, grants from Inmunotek, grants from Cassella-med GmbH & Co. KG, personal fees from Laboratoire de la Mer, personal fees from Sidroga, grants and personal fees from HAL BV, personal fees from Lek, personal fees from PRO-AdW ise, personal fees from Angelini Pharma, outside the submitted work.

000898 | Sensitization to dog and cat allergen components in a cohort of German allergic patients

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Background: The prevalence of animal sensitization has increased worldwide. Allergy to dogs and cats affect 10% – 30% of the population and is a growing public health concern for its involvement in the incidence of allergic respiratory diseases. Therefore, there is a need to accurately diagnose these patients and to develop optimized allergen extracts for personalized allergen immunotherapies. In this sense, molecular allergology offers new possibilities to improve the diagnosis. The aim of this study was to evaluate the sensitization profile to dog and cat allergens in a German cohort.

Method: Five hundred allergic patients from different regions of Germany were included in the study. The selection of patients was based on the diagnosis of allergy (case history, clinical signs and skin prick-tests results to aeroallergens). Sera samples were collected and analyzed by ImmunoCAP™ to determine the specific IgE levels to dog and cat epithelia. After this analysis, sIgE to dog and cat molecular allergens was determined.

Results: Out of the 500 subjects included in the study, 141 (28%) were sensitized to cat epithelium and 110 (22%) to dog epithelium. From the 141 patients sensitized to cat, only 5 (4%) were monosensitized and 80 (57%) of them, were also sensitized to dog. No monosensitized individuals were identified in case of dog sensitization. In cat allergic patients, the highest sensitization rate was observed for Fel d 1 (79%), followed by Fel d 7 (18%) and Fel d 4 (17%). Sensitization rate to Fel d 2 was low (3%). In dog allergic patients, the highest sensitization rate was observed for Can f 1 (32%), followed by Can f 6 (23%), Can f 5 (22%) and Can f 4 (15%). Sensitization rates to Can f 2 and Can f 3 were 7% and 6%, respectively. Regarding the major allergens, 70% of cat sensitized patients were monosensitized to Fel d 1. In dog sensitized patients, 21% and 17% were monosensitized to Can f 1 and Can f 5, respectively.

Conclusion: We obtained a complete sensitization map of cat and dog allergens in Germany, showing a high rate of polysensitization to household pets. This study highlights the importance of molecular diagnosis to facilitate personalized immunotherapy treatments.

Conflicts of interest: Prof. Dr. Mösges reports grants and personal fees from LETI, during the conduct of the study; personal fees from ALK, grants from ASIT biotech, personal fees from allergopharma, personal fees from Allergy Therapeutics, grants and personal fees from Bencard, grants, personal fees and non-financial support from Lofarma, non-financial support from Roxall, grants and personal fees from Stallergenes, grants from Optima, personal fees from Friulchem, personal fees from Hexal, personal fees from Servier, personal fees from Klosterfrau, non-financial support from Atmos, personal fees from Bayer, non-financial support from Bionorica, personal fees from FAES, personal fees from GSK, personal fees from MSD, personal fees from Johnson&Johnson, personal fees from Meda, personal fees and nonfinancial support from Novartis, non-financial support from Otonomy, personal fees from Stada, personal fees from UCB, non-financial support from Ferrero, grants from BitopAG, grants from Hulka, personal fees from Nuvo, grants and personal fees from Ursapharm, personal fees from Menarini, personal fees from Mundipharma, personal fees from Pohl-Boskamp, grants from Inmunotek, grants from Cassella-med GmbH & Co. KG, personal fees from Laboratoire de la Mer, personal fees from Sidroga, grants and personal fees from HAL BV, personal fees from Lek, personal fees from PRO-AdW ise, personal fees from Angelini Pharma, outside the submitted work.

001073 | Depigmented-polymerized phleum pratense and grass-mix extracts are similar in their tolerogenic capacity for use in allergen-specific immunotherapy treatments

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*Presenting author: N.A.N. Samson

Background: Chemically modified derivative of whole allergens, also known as allergoids, have been demonstrated to have superior safety while maintaining immunogenic profile. We have previously shown that grass pollen modified extract is hypoallergenic and can modulate T and B cell responses. Here, we hypothesize that both single grass or grass-mix pollen allergoids induce similar cellular and molecular mechanisms, making them both suitable for use in allergen-specific immunotherapy.

Method: Whole blood and peripheral blood mononuclear cells (PBMCs) were collected from 10 grass pollen allergics (GPA) and 5 non-atopic controls (NAC). The allergenicity of depigmented *Phleum pratense* (DPG Phlp) extract and depigmented-polymerized (DPG-POL) extracts of Phlp or Grass-mix (composed of 5 individual grasses), were measured by their ability to elicit basophil activation and histamine release using flow cytometry. Allergen-specific Th2A, Tfh cells and IL-10$^+$ Breg cells were quantified by flow cytometry. Single cell transcriptomic analysis using 10x Genomics was utilized to investigate the molecular mechanisms elicited by DPG-POL Phlp and Grass-mix in GPA (n = 3).

Results: Both DPG-POL Phlp and Grass-mix demonstrated reduced capacity to elicit basophil activation (CD63$^+$CRTh2$^+$; EC_{50} = 83.43 ± 4.92 ng/mL and 93.1 ± 2.93 ng/mL) and histamine release (DAO$^-$CD63$^+$CRTh2$^+$; EC_{50} = 103.80 ± 8.02 and 113.10 ± 10.05 ng/mL for DPG-POL Phlp and Grass-mix, respectively), compared to DPG Phlp. Both DPG-POL Phlp and Grass-mix had reduced capacity

to induce proliferation of Th2 (both, $p < 0.01$), Th2A (both, $p < 0.05$), IL-4$^+$ Tfh ($p < 0.05$) and IL-21$^+$ Tfh cells compared to DPG Phlp in GPA. Both DPG-POL Phlp and Grass-mix were more prominent in inducing CD19$^+$CD5^{hi}IL-10$^+$and CD19$^+$CD5^{hi}CD38^{int}CD24^{int}IL-10$^+$ Breg cell subsets compared to DPG Phlp extract in GPA (all, $p < 0.05$). These observations were supported by unbiased clustering analysis FlowSOM. Single cell transcriptomic analysis confirmed little to no difference in the molecular mechanisms underlying tolerance induction by the two modified extracts. Both DPG-POL Phlp and Grass-mix were associated with dampening of Th2-associated genes (*SOCS3* and *FOS)* and induction of immunoprotective CD52, compared to DPG Phlp.

Conclusion: Findings from this study confirmed that there is no difference between the two polymerised extracts with both DPG-POL Phlp and DPG-POL Grass-mix being potent modifier of the immune response and inducers of tolerance.

Conflicts of interest: R. Moya and J. Carnés are employees of LETI Pharma S.L.U. This work has been performed with a research grant from LETI Pharma via Imperial College London.

100523 | In vivo safety and efficacy of a plant-made monoclonal antibody for atopic dermatitis treatment

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*Presenting author: V. Gomord

Background: Monoclonal antibodies are used in immunotherapy. They currently represent 53.5% of the FDA approvals in the last four years. They are generally produced in Chinese hamster ovary (CHO) cells. However, this expression system has some concerns such as safety, risk of contamination, investment cost and is time-consuming for the upstream process development. Atopic dermatitis (AD) is a chronic, relapsing, eczematous, itchy skin condition associated with skin barrier dysfunction. This complex dermatological pathology has IL31 as one of a central immunomodulator and AD is currently being treated with mAbs able to neutralize it. However, the treatment of a 10kg dog, with a monthly injection, costs at least 1200€ per year. The use of plants for pharmaceutical and industrial protein production has recently emerged and affordable plant-based platforms present many advantages.

Method: A Mab was developed for its production in a plant-based system. This plant-made mAb was characterized, its biological activity and in vivo efficacy to control dogs pruritus were compared to the ones of commercial Lokivetmab produced in CHO cells. Twelve dogs were included in a double-blinded controlled studies using the IL-31 challenge model. The basal pruritus was assessed initially and dog were challenged with 4 µg/kg recombinant canine IL-31 produced also in plant. The mean pruritus recorded during two hours was considered for further comparisons. Six dogs were subsequently treated on Day 0 with the plant-made Mab while the other 6 received Cytopoint.

Results: Dogs treated with plant-made mAb have shown to get a same or better improvement than Cytopoint-treated ones after challenge with dog IL31. Mab injections were not associated with any side effects. At day 14 and day 30, concentrations of both Mab were not statistically different, illustrating a very stability of plant made mAb.

Conclusion: The study demonstrates the safety and efficacy of the newly developed plant-based monoclonal antibody to control pruritus. We have previously shown that this plant based platform can also produce unique ebioparticle based vaccine that can be used in integrated immunotherapy, (associating passive and active immunotherapies) opening many indications where long-lasting immune surveillance is required against a self-protein.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on anaphylaxis

001229 | Toward a precise concepts of phentoypes of hymenoptera venom induced-anaphylaxis: A real- life study

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Background: Hymenoptera venom-induced anaphylaxis (HVA) is one of the leading causes of anaphylaxis in western countries with a prevalence of 15.2% in the adults and one of main cause of death in some countries. However, precision on phenotypes at-risk is still imprecise. Using real-life data, our aim was to characterise phenotypes and endotypes at-risk of presenting HVA to suggest future prevention strategies.

Method: A historic prospective analysis was performed based on the Venom Allergy and Hypersensitivity Database (VAHD) of the Allergy Unit of the Hospital University of Montpellier, France. Data from patients consulting in the Unit were collected between 2010 and 2021. Analysis was done in 2021. Patients were clustered according to the severity grade of anaphylaxis – grade I–II of Ring & Messner as mild and grade III–IV as moderate-severe anaphylaxis. All informed consent was obtained. Statistics were calculated with R studio software. Results were significant if $p < 0.05$.

Results: 602 patients were recruited, 54.5% were men with a mean age of 42.3. 26.4% considered severe. Severe HVA was significantly prevalent in adults ($p < 0.000183$). 26.65% were occupational among which 71.3% occurred during beekeeping. Atopic diseases such as asthma and pollinosis, mastocytosis, and cardiovascular diseases were significant risk factors to severe cases ($p < 0.001$). Personal history of anaphylaxis was reported in 44.3%. Vespulas were

responsible for 33.5% of reactions (p = 0.007015) within 5 minutes (p < 0.01). Adrenaline was used significantly by 11.5% of the cohort. 74.5% of patients underwent monotherapy desensitisation

Conclusion: Our findings highlight main risk factors to enhance the prognosis of patients with HVA. Patients at-risk of developing severe HVA were characterized as men, working with Hymenoptera or performing frequent outside activities during summer, with atopic disease and/or previous history of anaphylaxis, underlying mast cell and cardiovascular conditions. Risk increases when the allergological work-up is not completed and if the patient does not carry the adrenaline auto-injector. Future action is to optimize care and prevention according to our results.

Conflicts of interest: The authors did not specify any links of interest.

000978 | Multiomics characterization of a dietary intervention model with pectins in a nsLTP food allergy model

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Background: There is increasing evidence to suggest that food allergy (FA) is associated with environmental factors such as diet. Thus, changes in nutrition may cause dysbiosis of the microbiome, that may in turn play a key role in the etiology of FA. Dietary fiber can change the composition of the gut microbiome and promote health. Pectin is a type of dietary fiber that can induce immune regulation. Therefore, the aim of this study was to investigate the effects of FA treatment, based on an intervention with pectin, using nsLTPs allergy as a model.

Method: A total of 34 nsLTP allergic patients (14–60 y.o.) with clinical history of FA and positive skin prick test and specific IgE to nsLTP (Pru p 3) were included. The control group consisted of 9 subjects (14–60 y.o.) who did not meet the inclusion criteria. Patients were orally administered one of two pectin varieties or placebo twice a day for two months and were divided into three groups (Active 1, n = 13; Active 2, n = 12; Placebo, n = 9). Sera samples were obtained before (T_0) and after the intervention (T_2) and were analyzed to perform targeted metabolomics on bile acids, short chain fatty acids (SCFA) and several inflammation-related mediators by liquid chromatography coupled to mass spectrometry (LC-MS); and proteomics analysis using multiplex proximity extension immunoassays (OLINK Target 96). To evaluate tolerance oral food challenge was performed after treatment.

Results: Specific serum metabolic and proteomic changes were observed between T_0 and T_2 after pectin dietary supplementation. Although no differences were found regarding bile acid metabolism, treatment with Active 2 showed decreased levels of sphingosine-1-phospate (S1P), propionic acid and protein concentration of INF-γ, IL7 and TSLP. On the other hand, isovaleric acid and proteins MCP-1 and MCP-2 levels decreased only in the Active 1 group, indicating that different transduction pathways are operating according to the type of intervention. In addition, the clinical efficacy of pectin to increase food tolerance to nsLTP-containing fruit such as peach, was evaluated. Metabolites such as betaine, LPC 19:0 and propionic acid; and proteins such as CXCL10 and CXCL11 were found altered between nsLTP tolerant and non-tolerant patients.

Conclusion: Our results provide evidence that dietary intervention with pectin induces differential metabolic and proteomic profiles in nsLTP-allergic patients, giving rise to elucidate new potential immunomodulatory mechanisms and therapeutic targets in FA.

Conflicts of interest: The authors did not specify any links of interest.

001017 | Anaphylactic reactions reduce circulating lipoproteins and impair HDL-mediated macrophage cholesterol efflux

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Background: Anaphylaxis is the most severe and life-threatening allergic reaction. Recognized molecular and cellular mechanisms do not cover the understanding of all the reactions. Moreover, clinical diagnosis will be widely benefited with the use of sensitive and specific biomarkers. We aimed to determine the amount of serum lipoproteins and apolipoproteins from anaphylactic patients and the ability of HDL to promote macrophage cholesterol efflux (MCE).

Method: For this purpose, different proteins were measured in the acute and basal phases of 115 anaphylactic patients (88 moderate reactions and 27 severe reactions) and in 38 patients with hypersensitivity reactions. Specifically, cholesterol, high-density lipoprotein (HDL), low density protein (LDL), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB), and triglycerides (TG). The MCE capacity of HDL from anaphylactic patients was determined using TopFluor-cholesterol-loaded J774.A1 macrophage cells. In addition, a mRNA screening from the main efflux/influx cholesterol receptors

was carried out by RT PCR from liver extracts of Active Systemic Anaphylaxis (ASA) mice.

Results: A significant reduction in the levels of HDL and LDL-cholesterol, ApoA1 and ApoB was observed in serum samples from severe anaphylactic reactions. Interestingly, an impairment of HDL-mediated MCE capacity was found in anaphylaxis. However, the evaluation of transcriptomic levels of influx and efflux receptors revealed increased levels of ABCA1 and ABCG1 in ASA livers, suggesting a possible systemic compensatory mechanism.

Conclusion: Although further investigation in this field is required, HDL and LDL-cholesterol levels appear as potential biomarkers of severe reactions. In addition, the deficient MCE capacity would be indicating a potential cardiovascular damage and inflammation associated to severe anaphylactic reactions.

Conflicts of interest: The authors did not specify any links of interest.

001032 | Endocan in anaphylaxis: Systemic and local microenvironment evaluation

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Background: A growing body of evidence points to the relevance of the endothelium in anaphylaxis. This cellular monolayer is protected by a dynamic microstructure of a carbohydrate mixture called the endothelial glycocalyx (EG) and its injury has been associated with endothelial dysfunction. In addition, EG disruption results in a source of biomarkers. Our previous studies demonstrated that the extracellular matrix and EG protein pattern of human microvascular endothelial cells is diminished in response to sera from anaphylactic patients. One of the proteoglycans from EG, endocan (ESM-1), has already been proposed as a biomarker of cardiovascular disease. Therefore, the aim of this study is to evaluate ESM-1 as a potential biomarker in the context of anaphylaxis.

Method: ESM-1 was quantified in a population of 105 paired sera samples from anaphylactic patients by ELISA. To mimic *in vitro* anaphylaxis, 10 human lung endothelial cell-sera systems were created. ESM-1 sera levels were measured before and after 2 hours of cellular contact.

Results: We did not found differences between the protein levels of ESM-1 in acute-phase sera from anaphylactic patients compared to their baseline values. Besides, there was no correlation with ESM-1 levels and the grade of severity of the reactions. However, the incubation of endothelial cells with sera from anaphylactic patients increases the release of ESM-1.

Conclusion: Although further research is required, the usefulness of ESM-1 as a biomarker seems scarce. Nonetheless, the increased release observed in the endothelial *in vitro* system, after anaphylactic sera samples contact, could suggest its role in local endothelial microenvironments.

Conflicts of interest: The authors did not specify any links of interest.

100060 | Health-related quality of life in adults with severe systemic peanut and tree nut allergy

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Background: Food allergy can negatively influence health-related quality of life (HRQL). Studies focussing on the HRQL of food allergic adults are scarce.

The aim of this analysis is to analyse the HRQL in adults with peanut and/or tree nut allergy by generic and disease specific HRQL-questionnaires and to compare their generic HRQL with healthy adults.

Method: The Food Allergy Quality of Life Questionnaire, Adult Form (FAQLQ-AF) and EQ5D5L were applied in patients with suspected or confirmed allergy to peanut or tree nut, all on a strict elimination diet. The FAQLQ-AF score (total and subdomains), the EQ5D5L descriptive part, visual analogue scale (VAS) and index values were analysed. The EQ5D5L questionnaire was also answered by a non-atopic healthy control group. Differences between groups were analysed using Wilcoxon-Rank-Sum-Test and Kruskal-Wallis-Test.

Results: 61 allergic patients with a median age of 28 years (interquartile range: 24–31), 39% male patients were compared to 65 controls (27 (22–32) years, 35% male subjects). 45 (74%) of the allergic patients had at least one physician confirmed peanut or tree nut allergy. Allergic adults reported significantly more complaints in the anxiety and depression domain of the EQ5D5L (any complaints: 43% compared to 15%, $p < 0.001$) and regarding difficulties in performing usual activities (13%/1.5%, $p = 0.015$). The EQ5D5L-Index value and VAS scale were significantly lower in the allergic group (Index: 0.97 (0.94–1.00)/1.00 (0.97–1.00), $p = 0.013$; VAS: 85 (75–93)/93 (90–98), $p < 0.001$), indicating a reduced HRQL.

The median FAQLQ score was 3.52 with the highest impairment in the emotional impact domain. Females had significantly higher results in the total FAQLQ score and most subdomains, indicating a greater impairment of HRQL. Within female but not male patients, a stricter avoidance of traces had a significant negative influence on HRQL.

Conclusion: We confirm the negative influence of peanut and tree nut allergy on HRQL in disease specific but also generic questionnaires. Sex specific differences are present, e.g., females experience a higher impact on HRQL than males and a stricter allergen avoidance further reduced HRQL. Efficacious and safe treatment

approaches are needed to improve the HRQL in peanut and tree nut allergic adults.

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Conflicts of interest: The authors did not specify any links of interest.

100111 | General use adrenaline (epinephrine) autoinjectors in new south wales (NSW) public schools

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Background: The public education system in NSW, Australia, educates 823000 students across 2220 schools. All school staff receive regular training to recognise and manage anaphylaxis. Staff are taught that anaphylaxis is usually rapid in onset and characterised by any potentially life-threatening compromise in breathing and/or circulation. When non-food triggers such as insects or ticks are implicated, abdominal pain or vomiting may indicate anaphylaxis. Since 2012 schools have been required to maintain at least one adrenaline autoinjector (AAI) for general use (GU) per school, in addition to a personally prescribed device for each student recognised as being at risk of anaphylaxis.

Method: Over the period January 2017 to December 2022 all reports of anaphylaxis and/or AAI use were followed up and reviewed by allergy nurses. Data collected included demographics, symptoms, known allergies, triggers, and type of treatment administered (personally prescribed / GU AAIs). Likelihood of true anaphylaxis/other diagnosis was assessed for each report.

Results: 692 episodes of anaphylaxis and/or AAI use were reported in NSW public schools over the 6-year period. A GU AAI was used in 294 instances (43%) as either an initial or subsequent dose. Reasons for use of a GU AAI include no known allergies prior to event 142 (48%); known allergies but no personally prescribed AAI 41 (14%); GU AAI used for second or subsequent dose 38 (13%); personal AAI prescribed but unavailable 47 (16%) [not provided to school 40 (14%), expired 6 (2%), cloudy 1 (0.3%), failed to fire 1 (0.3%)]; and pragmatic reasons 32 (11%) [GU AAI closer to student 30 (10%), GU AAI having imminent expiry date 1 (0.3%), personally prescribed AAI withheld to maintain availability during transport from remote location 1 (0.3%)].

Anaphylaxis was assessed as being the likely diagnosis in 232 (79%) of the events where GU AAIs were given. The most common trigger was food in 102 (35%) cases, unknown trigger but likely anaphylaxis 79 (27%), insect 39 (13%), medication 6 (2%), exercise 4 (1%) and other 2 (0.7%). The likely diagnosis in those events determined not to be anaphylaxis was anxiety 19 (6%), asthma 10 (3%), mild-moderate reaction 9 (3%), seizure 7 (2%), vocal cord dysfunction 3 (1%), other 14 (5%).

Conclusion: In at least a third of cases, GU AAIs enabled access to adrenaline for students who may have otherwise had delayed or no treatment for anaphylaxis. Availability of GU AAIs does not result in overtreatment with adrenaline.

Conflicts of interest: The authors did not specify any links of interest.

100132 | IGE- and IGG-driven anaphylaxis mechanisms in a murine model by lipidomics

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Background: Anaphylaxis incidence and severity have increased during the last years attracting the interest to understand their underlying molecular mechanisms. Its multisystemic nature and the heterogeneity of the reactions difficult to recognize their rapid onset becoming life-threatening. Traditionally, allergic (IgE-dependent) and non-allergic (IgE-independent) mechanisms have been recognized that probably lead to a differential functional impact on the homeostasis of the affected tissues. Lipids are bioactive molecules with a recognized role in inflammatory and immune responses including allergy. Therefore, the aim of this study was to characterize the lipidomic profile of two key organs in severe anaphylactic reactions (heart and lung) as well as in serum from experimental IgE- and IgGmediated passive systemic anaphylaxis (PSA).

Method: A mouse model of PSA was applied by using control and IgE- or IgG-sensitized muce. Twenty-nine samples from sera and tissues were collected after five, thirty or sixty minutes after challenge and body temperature registered to confirm anaphylaxis. The lipidomic profile of both serum and tissues were obtained using liquid chromatography coupled to mass spectrometry (LC-MS). Interpretation of the results is according to the time-course and between both mechanisms.

Results: Both IgE and IgG serum and tissues exhibit significant different lipid profiles along the time by using multivariate statistics ($p\,corr > 0.7$ and VIP score > 1.0). The highest differences between the three groups (Control, IgE and IgG) were reached at 5 min in the heart, whereas for serum was at 30 min, and for the lung was at 60 min after induced the challenge. Broadly, from all the biological systems used, data support to fatty acids (FA, e.g. FA 16:0, FA 20:0, FA 20:3, FA 22:5), as relevant in serum IgE-mediated anaphylaxis.

On the contrary, phosphocholines (e.g. PC 16:0_18:2), and sphingomyelins (SM, e.g SM 18:1_22:0) appear in IgG-mediated anaphylaxis.
Conclusion: This study evidence the specificity of lipid profiles accordingly to IgE or IgG anaphylactic mediated mechanisms in a PSA mice model. In addition, the lipid profiles are changed over both time and type of sample (serum and tissues). Our experimental findings will help to reach an enriched diagnosis and treatment of anaphylaxis.
Conflicts of interest: The authors did not specify any links of interest.

100199 | Consumer anaphylaxis simulation training for parents and families of children with food allergies

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Background: With increasing incidence of food allergy in children and the unpredictable nature of severity of allergic reactions, it highlights the need to educate parents and caregivers in managing anaphylaxis. Early recognition of anaphylaxis and prompt administration of adrenaline are essential to reduce morbidity and mortality. Parental anxiety and lack of confidence are barriers to the use of adrenaline autoinjectors (AAIs). Consumer Anaphylaxis Simulation Training (CAST) is a course that aims to optimise parent and caregiver knowledge and confidence in effective management of allergic reactions and anaphylaxis
Method: Participants were recruited from an allergy research expression-of-interest database. Participants completed an eLearning package using Articulate software program, followed by a clinician-led online simulation session focused on recognising the progression of an acute allergic reaction and appropriate management.
Storyboards for three anaphylaxis scenarios were developed for the simulation. A high-fidelity child mannequin was used for the simulation, complemented by audio-visual resources (photographs and videos of relevant signs and symptoms), enabling the participants to demonstrate recognition of key signs and symptoms, and management principles including correct posture and EpiPen administration. Baseline and 4-week post-course assessments of knowledge using multiple-choice questions, self-reported comfort with EpiPen administration (visual analogue scale, VAS), and parent empowerment (Food Allergy Efficacy Scale for Parents, FASE-P) were performed. Pre- and post-training scores were compared using a paired sample t-test. Feedback was sought from all participants after the course, including Net Promoter Score (NPS).
Results: 41 participants were enrolled in the study with 29 participants completing all components of the course and 3 withdrew before completing the online simulation session component. A summary of the demographics of the participants was shown in Table 1 (not included).

The median scores for baseline and 4-week post-course assessments of knowledge (MCQ) were 8.0 and 10.0 with a *p* value of 0.001. There were significant increases across all aspects of post-course VAS mean scores (confidence in recognizing anaphylaxis, knowing how and when to use an EpiPen) and FASE-P mean scores as shown in Figures 1 and 2. The Net Promoter score(NPS) based on responses to question 'how likely the participants will recommend the training course to a friend or family member who cares for a child with food allergy' was 89.3% with a mean NPS score of 9.41/10 (SD of 1.1). Participants reported that the course improved their understanding and confidence in managing allergic reactions and anaphylaxis and that small group simulation was conducive to learning compared to existing anaphylaxis and AAI education.
Conclusion: A multi-modal training program including eLearning package and clinician-facilitated online simulation sessions is a novel approach to deliver consumer education in management of allergies. CAST program is feasible and scalable, with participant feedback suggesting potential benefits for parents and caregivers of children with severe food allergy beyond existing approaches to consumer education.

Table 2
Summary of scores Baseline and 4-week post course

	Total	Pre	Post	Change	
	Number	Median (IQR)	Median (IQR)	Median Difference (95% CI)	p value
MCQ Score	35	8.0 (7.0, 9.0)	10.0 (9.0, 10.0)	1.0 (1.0 to 2.0)	<0.001
VAS	Number	Mean (SD)	Mean (SD)	Mean difference (95% CI)	p value
How confident do you feel in knowing which treatment to choose for your child	34	63.6 (18.3)	78.9 (16.9)	15.3 (8.8 to 21.8)	<0.001
How confident do you feel in recognising anaphylaxis?	34	58.5 (18.2)	78.6 (14.5)	20.2 (12.4 to 28.0)	<0.001
How confident do you feel in knowing how to use an EpiPen?	34	69.5 (23.3)	85.6 (13.8)	16.1 (9.9 to 22.3)	<0.001
How confident do you feel in knowing when to use an EpiPen?	34	54.2 (20.0)	77.7 (14.9)	23.5 (17.0 to 30.0)	<0.001
How confident do you feel in knowing what to do after you administer an EpiPen?	34	62.0 (22.3)	83.9 (16.9)	21.9 (14.3 to 29.4)	<0.001
How confident do you feel in knowing where to access further information on anaphylaxis	34	59.0 (20.1)	81.9 (15.9)	22.9 (14.8 to 31.0)	<0.001

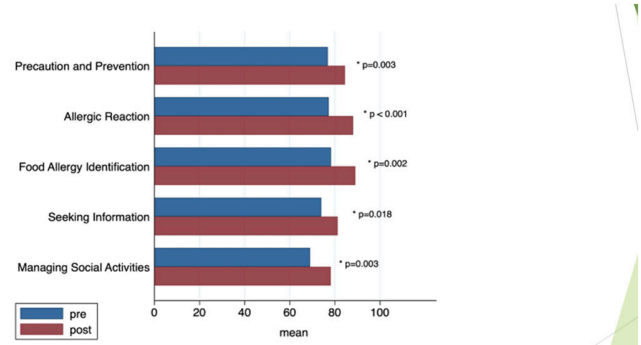

Figure 2.
Mean Differences for Baseline and 4-week Post-course FASE-P Scores (Food Allergy Self-Efficacy Scale for Parents (FASE-P)

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on allergy diagnosis I

001163 | Analytical and clinical performance of a novel chemiluminescent microparticle immunoassay for detection of tryptase

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Background: During an anaphylactic reaction or other reaction leading to clinical symptoms caused by mast cell degranulation, serum total tryptase concentrations usually increase substantially above baseline. Chronic mast cell activation is more difficult to diagnose because in some of these patients the tryptase levels are constantly elevated and may point to an occult form of mastocytosis. The most widely used approach to determine tryptase levels is by immunoassay. Here we introduce a novel, high throughput automated platform that utilizes magnetic microparticles in combination with fluorescence and chemiluminescence signals to quantify tryptase present in human serum. We demonstrate the analytical and clinical performance of the new chemiluminescent microparticle immunoassay for detection of total tryptase levels in this study.
Method: The precision and functional sensitivity of the tryptase chemiluminescent microparticle immunoassay were evaluated in accordance with CLSI EP05-A3. Limit of Blank (LoB) and Limit of Detection (LoD) were estimated in accordance with CLSI EP17-A2. Assay linearity was assessed in accordance with CLSI I/LA20-A3. Cross reactivity of potential endogenous and exogenous interferences was evaluated in accordance with CLSI EP07-A2. Method comparison against a commercially available tryptase assay was performed in accordance with CLSI EP09-A3 and CLSI EP24-A2.
Results: The chemiluminescent microparticle immunoassay analyzer produced overall repeatability of <8% CV and within-lab precision of <10% CV for the tryptase assay. Functional sensitivity was determined to be excellent with LoB and LoD of <1 µg/L across multiple instruments and reagent lots. The performance of the assay exhibited good linearity across the reportable range of 1–200 µg/L. No significant reactivity was observed for cross reactive, endogenous, and exogenous potentially interfering substances. The system also generated acceptable correlation when compared to a commercially available tryptase assay on over 100 human serum samples.
Conclusion: The tryptase assay on the chemiluminescent microparticle immunoassay analyzer exhibited strong analytical and clinical performance for the determination of tryptase level in human serum samples.
Conflicts of interest: The authors did not specify any links of interest.

000949 | Dendritic cells immunophenotype in patients with hypersensitivity to titanium and its oxide

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Background: Titanium (Ti) is a metal with protective titanium dioxide (TiO_2) film on its surface. Ti often used in medical implants while TiO_2 is a widespread dye of food, drugs, toothpaste and cosmetics. Hypersensitivity to Ti is accompanied by macrophage activation and secretion of pro-inflammatory cytokines (IL-1β, TNF-α, IL-17).
Method: 31 people were examined (18 women (58%), 13 men (42%)): 11 (35%) – had prostheses with Ti, 12 (39%) – reacted to metals, 18 (58%) – reacted to cosmetics, 20 (65%) – had allergic anamnesis to other agents. Hypersensitivity to TiO_2 according to the anamnesis was in 19 (61%) patients. Blood was taken before and after oral provocation test with 2 mg of particles used in the food industry ("food") of TiO_2. PMBC were isolated by centrifuging the sample on a Ficoll-Pak density gradient (1077 g/L). Monocytes were obtained from the PMBC fraction by the adhesion method and were cultivated to dendritic cells (DC) by incubation in AIM-V medium with 1.5% autoserum (120 µL per 8 mL), 50 ng/mL GM-CSF and 25 ng/mL IL-4 was for 6 days in a CO_2 incubator at 37°C. Whole blood cells before and after the provocation and cultured DC obtained from blood after provocation (cDC_{pr}) were phenotyping with fluorescent antibodies to $CD209^+$, $CD85^+$, $CD273^+$, $CD274^+$, $IFNg^+$ by flow cytometry. To assess TiO_2 effect in vitro, cultured as described above DC from donors' blood were incubated for 24 h at 37°C in a medium containing 10 µg/L of nano-, micro and "food" particles of TiO_2.
Results: In patients with suspected intolerance to Ti and TiO_2, the absolute and relative $CD209^+$ cells number in blood was lower than in those without allergy to Ti (*T*-test: $p = 0.01$, $p = 0.01$), as well as the absolute number of activated $CD209^+CD85^+$ (*T*-test: $p = 0.01$) and $CD209^+IFNg^+$ cells from blood (*T*-test: $p = 0.01$). In patients with reactions to metals in anamnesis, the absolute number of $CD209^+273^+$

cDC_{pr} was lower than in controls (M-U: $p = 0.03$), as well as the absolute number of $CD209^+273^+274^+$ cDC_{pr} (M-U: $p = 0.03$).

Analysis of the fluorescence intensity showed that exposure to all three types of TiO_2 particles reduces $CD209^+$ cells number (Wilcoxon: $p < 0.05$). The maximum effect was shown for TiO_2 nanoparticles.

Conclusion: Data obtained suggest that hypersensitivity to titanium and its oxide can be associated with decreasing number of $CD209^+$cells and activated $CD209^+CD85^+$ and $CD209^+IFNg^+$ DC in blood, which correspond to the in vitro results. Metal allergy can cause decreasing of cultured DC obtained after provocation with TiO_2.

Conflicts of interest: The authors did not specify any links of interest.

001653 | Natural history and relationship of serum immunoglobulin a responses to aspergillus fumigatus extracts and components in pediatric cystic fibrosis patients

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Background: Cystic fibrosis (CF) is an inherited condition predisposing to *Aspergillus fumigatus* (AF)-induced pulmonary disease, including life-threatening allergic bronchopulmonary aspergillosis. Humoral responses to AF are currently monitored with serum IgE and IgG quantification, but specific IgA are usually not assessed. However, a protective role for AF-IgA has been suggested. Here, we describe the natural history of AF-specific IgA responses in a pediatric CF cohort.

Method: IgA and IgE determination to AF extract and components Asp f 1, Asp f 2, Asp f 3, Asp f 4, and Asp f 6 (ThermoFisher Scientific, Phadia, Sweden) were assessed in a cohort of 84 consecutive CF patients undergoing routine monitoring for total IgE and AF-specific IgE between July 2015 and September 2018 in the competence center for pediatric CF from the University Hospital of Marseille (France). AF-specific IgA were measured retrospectively on excess serum samples. Clinical data were retrospectively collected.

Results: The cohort comprised 36 males (43%) and 48 females (57%), with a median age of 13 years (range 9 months to 18 years), of whom 35 had detectable AF-specific IgE. In non-sensitized subjects, the prevalence of AF-specific IgA increased with age: 6% (0–4 years), 47% (5–9), 70% (10–14), 100% (15–18), $p = 0.0002$. AF component-specific IgA followed the same pattern, with Asp f 1 the apparent immunodominant allergen, followed by Asp f 2 and Asp f 6 with a maximum of 50% respectively, while Asp f 3 and Asp f 4 reached prevalence levels of 20%–25%. AF sensitization was associated with increased prevalence and levels of AF-specific IgA (extract and components). Levels of AF-specific IgE and IgA showed a small but significant correlation (Spearman r 0.3, p 0.02). Two children had active ABPA at the sampling time and displayed moderate levels of AF-specific IgA (6 mgA/L).

Conclusion: We describe here the natural evolution of serum AF-specific IgA to extract and components in a pediatric CF cohort aged 9 months to 18 years, reporting that the prevalence and levels of serum AF-specific IgA increase with age and are associated with AF-specific IgE responses, however their molecular IgA profile is different from IgE, especially in terms of prevalence of Asp f 2, Asp f 4 and Asp f 6.

Conflicts of interest: J.vitte has received speaker and consultancy fees from Astra Zneca, Meda Pharma (Mylan), HpVac, Stallergenes-Greer, Thermo Fisher Scientific in the past 5 years.

000938 | Novel skin prick automated test device contributes to standardization of allergy diagnosis

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Background: The skin prick test (SPT) is the gold standard for identifying allergic sensitization in individuals suspected of having an aeroallergy. Recently, it was demonstrated that SPT via a novel skin prick automated test (SPAT) device showed increased reproducibility and tolerability compared to conventional SPT besides other benefits (Gorris et al., Allergy, 2022). This study aimed at evaluating prick location bias using the novel SPAT.

Method: The 118 volunteers enrolled in the study underwent SPAT with histamine (9 pricks) and glycerol control (1 prick) solutions. Readout was performed by the SPAT device and maximal wheal sizes were determined by the physician on the computer. Prick location bias was assessed along the medial vs lateral and proximal vs distal axes on the forearm.

Results: In total 944 histamine pricks were analysed. Four medial and 4 lateral histamine pricks were grouped and wheal sizes were compared. Maximal wheal sizes were not significantly different between medial and lateral prick locations ($p = 0.41$). Histamine pricks were grouped by 2 based on their position on the proximal-distal axis on the forearm. There was no significant difference between the 4 groups of prick locations analysed ($p = 0.73$).

Conclusion: Prick location on the forearm did not influence wheal size measurement of SPAT. SPAT contributes to standardization of SPT for allergy diagnosis.

Conflicts of interest: This study was supported by VLAIO grant (HBC.2021.1170). SG, DL and SFS are employees of Hippocreates. SFS, SG, RD and LVG hold shares of Hippocreates who developed the SPAT device.

001262 | Ratio of total ige to PruP3 value is associated with clinical severity of lipid transfer protein allergy in the west of scotland anaphylaxis service

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Background: With emerging data on LTP allergy in Northern Europe, we aim to interrogate clinical and molecular signature of LTP allergy in a cohort of patients diagnosed through the West of Scotland Anaphylaxis Service (WSAS).

Method: We interrogated the WSAS records between 2017–present to identify demographics and clinical spectrum of LTP allergy, alongside clinical utility of PruP3 specific IgE testing and the use of objective tests (Total IgE to PruP3 ratio) as a potential marker of severity or pattern of clinical reactions.

Results: We identified 35 patients diagnosed with LTP allergy. Patient group included 15 male and 20 female patients, with average age of 32 (±10.2) years. Majority of patients had prior diagnoses of atopy (85.6%), particularly hay fever (62.9%).

Clinical presentations included 65.7% patients with oral allergy syndrome, while 88.5% had systemic symptoms and 57.1% had confirmed anaphylaxis. Among patients with systemic reactions, 40% had delayed reaction by median of 60 min (40–240 min). Reactions were most commonly provoked by consumption of rosacea fruit (66%) or nuts (42.9%). Regardless of clinical trigger for LTP allergy, 94.3% of patients had positive PruP3 specific IgE on serum testing. Higher PruP3 serum values were associated with severe reactions, such as anaphylaxis (5.9 ± 5.4 kU/L in mild cases vs 14.4 ± 16.9 in the anaphylaxis group). Reciprocally raised total IgE was found predominantly in patients with mild symptoms, with significant difference in the ratio of total IgE to PruP3 (1106 ± 1441 in mild cases vs 109.3 ± 164.3 in patients with anaphylaxis, $p = 0.01$).

Conclusion: Patients diagnosed with LTP allergy in WSAS presented with a spectrum of clinical features and were unified by predominantly positive PruP3 serum testing. Severity of reaction was associated with higher PruP3 values and lower total IgE levels, thus identifying a total IgE to PruP3 ratio as a potential serological marker in this cohort.

Conflicts of interest: The authors did not specify any links of interest.

000819 | Validation of reference values and suggested clinical threshold for serum total IGE

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Background: One of the most cited studies regarding total IgE reference values is the one by Zetterström and Johansson from 1981, in which they measured serum IgE using Phadebas IgE PRIST in samples collected 1974 from adult non-allergic individuals in Uppsala. They reported an upper limit of normal [ULN] of 114 kU/L based on the geometric mean (13.2 kU/L) plus 2 standard deviations (SD) and proposed that IgE above 100 kU/L in patients with allergy-like symptoms was a strong indication for an atopic disease. It has been argued that these old reference values and suggested threshold are no more valid. The aim of the present study was to validate the reference values and suggested clinical threshold for serum IgE in non-atopic, apparently healthy, Uppsala subjects using the ImmunoCAP Total IgE assay.

Method: IgE was measured in two Uppsala cohorts from 1997 (Blood bank cohort) and 2011–2013 (ECRHS III cohort) using ImmunoCAP Total IgE. Atopic subjects (Phadiatop-positive, both cohorts) as well as subjects who reported a doctor's diagnosis of asthma or allergy-like symptoms (hayfever, rhinitis or rash) (only the ECRHS III cohort) were excluded from the reference value calculations. In accordance with the 1981 study, ULN was defined as the geometric mean + 2 SD. Arbitrary value imputation of IgE results below the limit of quantitation (LOQ = 2 kU/L) were done with either: (1) LOQ, (2) LOQ/√2, or (3) LOQ/2. The performance of 100 kU/L as a suitable threshold value for total IgE was studied in the ECRHS III cohort.

Results: The geometric means of total IgE (influenced by imputation method) were 16.9–17.4 kU/L (Blood bank cohort, $n = 63$) and 10.7–11.6 kU/L (ECRHS III cohort, $n = 113$) (overall mean: 14.2 kU/L). The ULN values were 113–130 kU/L (Blood bank cohort) and 104–128 kU/L (ECRHS III cohort) (overall mean: 118 kU/L). The clinical sensitivity and specificity of the 100 kU/L IgE threshold were 37.8% and 94.3% for atopy, 34.9% and 89.5% for doctor's diagnosis of asthma, and 24.5% and 97.3% for any reported allergy (asthma, hayfever, rhinitis or rash).

Conclusion: The reference values for total IgE reported by Zetterström and Johansson in 1981 are still valid and suitable also for the ImmunoCAP Total IgE assay. The proposed IgE threshold value of 100 kU/L showed a low sensitivity but high specificity for atopy, asthma, and allergy in the ECRHS III Uppsala study.

Conflicts of interest: Robert Moverare is employed by Thermo Fisher Scientific.

001363 | Protein G'-grafted mesoporous silica nanoparticles with varying pore sizes as an igg capture system in the context of in vitro allergy diagnosis

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Background: Immunoglobulin G (IgG)-binding particles can be used for IgG purification or to process clinical samples for diagnosis. High serum IgG levels can hamper allergen-specific IgE (sIgE) detection, main biomarker for *in vitro* allergy diagnosis. Although some materials for IgG capture are commercially available, they present a low IgG removal capacity, preventing their use in the clinic. In this work, we prepared mesoporous silica nanoparticles (MSNs) with different pore sizes, to which we grafted IgG-binding protein G'.

Method: Protein G'-grafted mesoporous silica nanoparticles were prepared in different steps: (a) synthesis by a biphasic water/cyclohexane method using tetraethylorthosilicate as silica precursor and cetyltrimethylammonium chloride as the structure-directing agent; (b) surfactant extraction with an ethanolic solution of ammonium nitrate; (c) amination with 3-aminopropyltriethoxysilane in toluene; (d) carboxylation with succinic anhydride in tetrahydrofuran; (e) protein G' anchoring by carbodiimide chemistry. Their IgG capture capacity was evaluated by Nanodrop (with known IgG concentration in PBS) or ELISA (with sera from healthy controls and allergic patients). The effect of IgG removal on *in vitro* sIgE detection was evaluated in sera from allergic patients using ImmunoCAP Phadia.

Results: MSNs with 4 different pore sizes (5–15 nm) were obtained and characterised. We found that for one optimal pore size (12 nm), the IgG capture capacity was greatly enhanced, achieving a 5-fold improvement compared to 2 state-of-the-art commercial systems (93.21% IgG removal *vs* 16.73%). The capacity of this material to selectively and efficiently capture human IgG (compared to IgE) was demonstrated in both solutions of known IgG concentrations as well as in human sera. Moreover, IgG removal from human sera from both controls and patients allergic to *Vespula vulgaris* venom was achieved using a fast single-step incubation protocol. Interestingly, IgG removal using the best-performing material enhanced *in vitro* IgE detection in sera from patients allergic to amoxicillin, with 2 out of 8 previously-confirmed allergic patients switching from a negative result by ImmunoCAP (sIgE <0.35 kU/L) to a positive result.

Conclusion: The results presented here highlight the great translation potential of optimised protein G'-grafted MSNs in the context of IgG removal for *in vitro* allergy diagnosis.

Conflicts of interest: J.L.P., T.D.F, M.I.M, C.M. and M.J.T. have a patent application (P202230701) pending, which is related to the work reported in this article. The rest of the authors declare no conflict of interest.

Flash talks on asthma

001119 | Correlates of barriers to PROMs use among physicians who use PROMs for atopic dermatitis and chronic urticaria

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Background: Patient-reported outcome measures (PROMs) are effective tools for monitoring chronic urticaria (CU) and atopic

dermatitis (AD). However, their use is still very low. The current study aims to identify the main correlates of barriers to POMS use observed by AD (atopic dermatitis) and CU (chronic urticaria) PROM users.

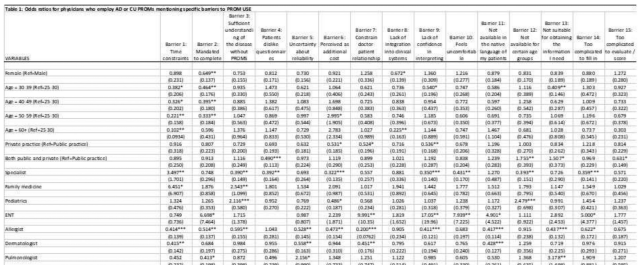
Method: We developed a questionnaire comprising three main aspects: (1) demographics, (2) knowledge about PROMs, and (3) PROMs perceptions and barriers. In the questionnaire, we asked if they used PROMs for specific dermatological or respiratory allergic diseases. For this analysis, we restricted the sample to physicians who use PROMs for atopic dermatitis and chronic urticaria. Then we employed logistic regressions with each barrier to PROM use as the dependent variable and demographic variables as the model covariates.

Results: The final analytical sample was 478 (physicians who used AD or CU PROMs). The most common barriers were time constraints, lack of integration into clinical systems, and unavailability for certain age groups. They had a median of 48 years old and 20 years of specialty.

Logistic regression demonstrated that being male was related to decreased odds of answering, and that lack of integration into the clinical systems was a barrier to PROM use. Also, older physicians had decreased odds of seeing time constraints as a barrier, but they also had higher odds of having costs due to PROMs as a barrier. Compared to doctors in public practice only, those who were in private practice were less likely to say that additional costs were a barrier to PROM use.

Specialists were more likely to consider time constraints as a barrier, but they were likely to consider as a barrier sufficient understanding of the disease without the need for PROMs, the thought that patients dislike PROMs, costs bringing additional costs, and that they are too complicated to fill.

Conclusion: CU and AD groups promote PROMs, but their use is minimal. Age, specialty, and sex affect physicians' perceptions of PROM usage barriers.



Conflicts of interest: The authors did not specify any links of interest.

001620 | Omalizumab tapering and discontinuation in severe chronic urticaria

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Background: Omalizumab has been widely used in the treatment of severe Chronic Urticaria (CU) for several years and tapering and discontinuation of omalizumab has been propose by several groups in the literature. However, identifying biomarkers of response to omalizumab and of predictors of discontinuation of omalizumab is still an unmet need. We aim to identify possible biomarkers in a Portuguese Immunoallergology Center.

Method: Retrospective review of patient with severe CU treated with omalizumab between January of 2015, and January 2023. Dose reduction was achieved by increasing the time interval between omalizumab administrations. Demographic information as well as treatment schedules, clinical evolution and analytical results were analyzed. SPSS V27 was used for statistical analysis, and $p < 0.05$ was considered significant.

Results: There was a total of 56 patients, 40 women (71.4%). The mean age was 41.56 ± 16.41 years-old. Thirty-eight patients (67.8%) had chronic spontaneous urticaria, 10 (17.8%) had mixed CU, and 8 (14.2%) had inducible chronic urticaria (4 patients had cholinergic urticaria, 2 cold urticaria, 1 heat urticaria and 1 delayed pressure urticaria). The average baseline UCT and UAS7 were 6 ± 3.72 and 15 ± 9.0, respectively.

The standard omalizumab dose was clinically effective (UAS7 < 6) in 41 patients (71.9%). Of those, 23 (56.1%) patients successfully reduced omalizumab dose. 4 patients (9.8%) discontinued omalizumab without having to restart it, but nineteen (46.3%) returned to the previous dose.

The mean time until a successful first omalizumab dose reduction was 72 weeks.

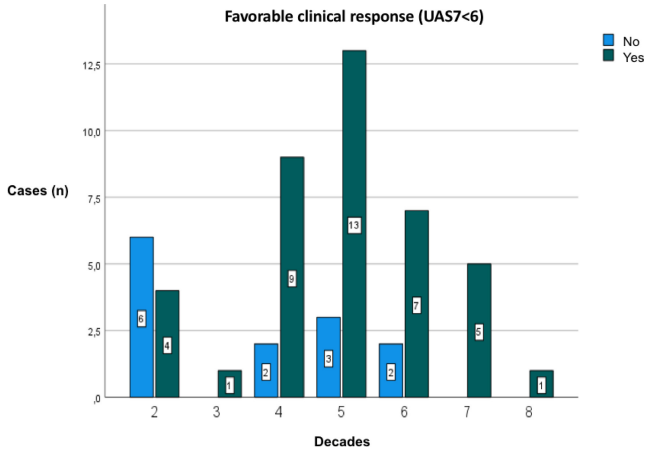
Patient age and a favorable clinical response (UAS7 < 6) had a positive correlation (Rho = 0.7; $p = 0.004$). The age of the patients was also correlated to the time interval until a dose reduction was tolerated (R = 0.69; $p = 0.005$).

The Sedimentary Rate (SR) was negatively correlated with the time interval until the first dose reduction (R = −0.89; $p = 0.007$). A positive correlation was found between the Basophil cell count and the same time interval until the first dose reduction (R = 0.69; $p = 0.0040$).

Conclusion: In our cohort, omalizumab treatment controlled the CU in roughly two-thirds of the cases. Furthermore, half of these patients tolerated a dose reduction in omalizumab while still maintaining the disease control.

Older patients showed a higher frequency of response to omalizumab (UAS7 < 6). However, increasing age was associated with a longer time interval until successful dose reduction was achieved.

A higher baseline SR was associated with a faster response to treatment, and a higher basophil cell counts appears to indicate a slower response.



Patient age and a favorable clinical response (UAS7 < 6) had a positive correlation (Rho = 0.7; $p = 0.004$). Older patients showed a higher frequency of response to omalizumab (UAS7 < 6).

Conflicts of interest: The authors did not specify any links of interest.

001655 | Omalizumab updosing in chronic spontaneous urticaria non-responder patients

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Background: Chronic Spontaneous Urticaria (CSU) is a major burden on 0.5%–1% of the global population. Although licensed dosing of omalizumab has been shown to be safe and effective in second-generation antihistamine refractory patients, not all patients achieve complete control. The goal of this study was to assess the efficacy and safety of omalizumab updosing in a small group of CSU patients.

Method: Patients with CSU treated with omalizumab between 2015 and 2023 were studied retrospectively. Demographic information, analytical parameters, as well as UCT and DLQI scores, were gathered. To facilitate analysis, therapeutic doses were expressed as mg/week. For statistical analysis, SPSS V27 was used.

Results: Twelve of 56 patients treated with 75 mg/week omalizumab did not respond to the standard therapeutic dose. They ranged in age from 12 to 59 years (mean 31.2 ± 17.7), with 8 (66.7%) being female. They were all updosed to 100–150 mg/week, and 7 (58.3%) achieved disease control. Dose reduction was tried in three people, and two of them tolerated it. Currently, all well-controlled patients have UCTs greater than 12 and DLQIs less than 0; in poorly controlled patients, the mean UCT is 6.6 ± 4.3 and the mean DLQI is 10.4 ± 7.4. When compared to responder patients, non-responders had more than double the eosinophil and basophil counts. The total treatment time ranged from 60 to 323 weeks, with a mean of 151.4 ± 83.9.

Conclusion: In patients with CSU refractory to standard dose, omalizumab updosing was associated with a complete response rate of 58.3%, with no adverse events. Higher eosinophil and basophil counts appear to be associated with a poor response to dosing increase.

Conflicts of interest: The authors did not specify any links of interest.

000211 | Rotational thromboelastometry profile in children with chronic spontaneous urticaria

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Background: Chronic spontaneous urticaria (CSU) is a common skin disorder characterized by spontaneously appearing wheal with itch and pruritus anywhere on the body for 6 weeks or longer. It has been proven that CSU is related to the generation of thrombin, the final enzyme of the coagulation cascade, and that the severity of the disease is paralleled through the amount of thrombin generated. Rotational thromboelastometry (ROTEM) assay enables the global assessment of coagulation status. In the present study, we aimed to test the coagulation profile in children with CSU using ROTEM and correlate these parameters with those of a healthy group.

Method: A total of 24 children with active CSU (11 girls and 13 boys) 8 to 17 years of age and age-matched and sex-matched 30 healthy control participants were enrolled in the study. ROTEM assays (intrinsic thromboelastometry and extrinsic thromboelastometry) were used to measure and analyze coagulation time, clot formation time, and maximum clot firmness.

Results: There was no significant difference in age and sex between the groups. Hematologic parameters that affected the ROTEM (erythrocytes, neutrophils, and platelets) were compared in patients with CSU and controls. There was no difference between the 2 groups in the following parameters: PT, aPTT, and fibrinogen levels. When ROTEM parameters were analyzed, there was no significant difference between the two groups.

Conclusion: According to our results, ROTEM plays no role in diagnosis or ruling out hypercoagulability in the CSU. Many more studies are needed before a conclusion can be reached on this topic.

Conflicts of interest: The authors did not specify any links of interest.

000952 | What topics are doctors most interested in learning about patient-reported outcomes (PROM) when addressing patients with chronic urticaria or atopic dermatitis?

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Background: CU and AD are prevalent chronic skin illnesses that burden patients. PROMs are recommended for daily clinical practice in both illnesses. However, its utilization is low, one of the reasons is its lack of knowledge. Our goal is to present the key areas in which physicians who treat CU or AD patients desire PROMs training and determine if there is a correlation with certain physician characteristics.

Method: We asked physicians who treated CU or AD "Which of the following areas would you like to receive further training/information about PROMs?". Logistic regressions were performed, with each topic considered as a dependent variable and the age and gender of the doctor, the specialty, years of professional practice, and type of care as independent variables, after adjusting for other confounding variables.

Results: 2528 medical professionals worldwide were surveyed. We found being female increased the odds of being interested in learning in how to choose a PROM, how to calculate and interpret PROMs scores (OR 1.8, 1.6, 1.7 respectively). Being ≥60 years old, increased the chances of interest of how to administer PROMs (OR 4.4). Having practice in a public and private consultation increased the odds of being interested in the benefits (OR 1.4) and challenges (OR 1.5) of using PROMs, and having private only practice, increased the chances of being interested in how to choose a PROM (OR 2.05). Regarding specialty, being Allergist and/or Dermatologist, has between 40 to 70% less chance to be interested in any further training about PROMs. Conversely, being a Family Doctor, increased the odds of being interested in how to administer PROMs (OR 2.8) and how to interpret them (OR 5.7). The other variables had no effect on the areas of interest mentioned.

Conclusion: These results suggest that being female, neither an allergist nor a dermatologist, and older increases the likelihood of pursuing PROM training. This paves the way for initiatives by various scientific societies to continue training on the benefits of PROM use, how to select, calculate, and interpret them, and to develop techniques to capture the interest of physicians who do not desire training on this matter.

Table 1. Adjusted Logistic Regression predicting the interest of physicians to receive further training about PROMs according to sex, age, specialty, type of consultation and years of specialty.

Variables	The benefits of using PROMs	The challenges of using PROMs	How to choose which PROM to use	How to administer PROMs	How to calculate PROM scores	How to interpret PROM scores	Other
Sex							
Female	1.251	1.299	1.812**	1.194	1.606**	1.742**	0.913
Age							
30-39	0.635						
40-49	0.926	0.911	1.420	1.485	0.617	1.111	0.139**
50-59	0.881	0.546	1.369	1.726	0.913	1.948	0.414
60+	2.134	0.524	1.063	1.647	0.758	1.407	0.398
		1.603	1.858	4.400**	1.180	1.210	18.95
Type of consultation							
Private practice							
Both public and private	1.159	0.932	2.057*	1.165	0.908	1.143	0.384
	1.474*	1.589*	1.385	1.205	1.291	1.385	1.587
Specialist, Yes	0.821	1.115	0.659	0.484*	0.501	0.549	0.284
Specialty							
Family Medicine	2.069	1.386	2.843	2.863**	2.148	5.779**	10.47***
Pediatrics	1.078	0.548**	0.928	1.154	1.536	1.271	0.898
ENT	3.062	0.895	2.165	0.993	0.804	1.550	35.66**
Allergist	0.301***	0.441***	0.423***	0.516**	0.456***	0.335***	1.217
Dermatologist	0.682	0.673	0.493**	0.743	0.456***	0.402***	3.904*
Pulmonologist	1.106	1.804	0.955	0.812	0.635	0.641	
Other	0.835	0.542*	0.614	0.882	0.448**	0.511*	1.1824
Years of specialty							
20-29	1.101	0.955	1.300	0.864	1.046	1.063	0.844
30-39	0.673	1.177	1.335	0.737	0.890	0.863	0.354
40+	0.452	0.720	0.909	0.661	0.630	1.051	0.014**

*** p<0.01, ** p<0.05, * p<0.1

Conflicts of interest: The authors did not specify any links of interest.

000824 | Identification of biomarkers for treatment duration and controller dose of omalizumab in patients with chronic spontaneous urticaria

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Background: Omalizumab (OMA) is effective in chronic spontaneous urticaria (CSU) patients, but some individuals do not respond to the standard dose (300 mg/month) or require treatment for a longer period than that indicated in the data sheet (6 months). The goal of this study was to identify biomarkers predictive of the need for OMA treatment longer than 6 months, or with >300 mg/month in CSU.

Method: Prospective study of CSU patients who received OMA in the Allergy Unit of Hospital Regional Universitario de Malaga in 2021. Clinical and analytical data was entered in BIOBADALER RedCap database.

Results: 94 patients (20.2% male, mean age 43.3 years) received OMA for CSU in 2021. 95% achieved control (UAS7 < 7) with OMA (83.2% of them with 300 mg/month and 16.8% of them with > 300 mg/month). Treatment duration in responder patients who maintained control after OMA discontinuation (15%, responder in remission, RRs) was 28 months on average. Responder individuals who required treatment to maintain control (44%, active responders, ARs) had been on OMA for 50 months and received 250 mg/month at the end of the study period on average. Compared to ARs, RRs presented higher serum total IgE at baseline ($p < 0.01$). Compared to patients who achieved control with 300mg/month, subjects requiring >300 mg/month had more hypothyroidism ($p < 0.01$), less NSAID-exacerbated cutaneous disease (NECD) ($p = 0.03$), more anti-TPO antibodies detectable in serum ($p < 0.01$) and lower blood basophil count (BBC) ($p = 0.02$) at baseline.

Conclusion: OMA induces control in 95% of CSU patients. Serum total IgE could serve as a biomarker for treatment duration, whereas hypothyroidism, serum anti-TPO antibodies, BBC and NECD could serve as a biomarker for OMA dose required for control.

Conflicts of interest: The authors did not specify any links of interest.

001142 | Natural course of acute urticaria and predictive factors associated with progression to chronic urticaria: Initial results of a prospective study in the emergency department of a tertiary university hospital in Greece

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Background: Acute Urticaria (AU, wheals and/or angioedema lasting < 6 weeks) has a lifetime prevalence of up to 20% and is characterized by a benign and self-limiting course, while in most cases, no clear trigger is identified. Data regarding the natural course of AU remain scarce. The present study aimed to identify progression rates of AU to CU and possible predictive factors related to the duration of the disease in patients visiting the emergency department (ED) of a tertiary hospital in Greece due to AU.

Method: Prospective study of patients visiting the Dermatological and/or Allergy ED of General University Hospital "Attikon", in Athens, Greece, from 06/2020 to 11/2022 due to AU. In all patients meeting the inclusion criteria (physician-diagnosed AU but not anaphylaxis), we recorded: A/a structured questionnaire including demographic data, time of episode onset, possible causes, personal history, medication, previous episodes of AU, previous visits to the ED, B/basic laboratory testing as indicated and C/follow-up remotely 15 and 45 days after the ED visit.

Results: A total of 247 patients [46.2% male, mean age 41.3 years ±15.9 (range: 16–90 years)] were included in the study. The mean time from symptoms onset to ED visit was 64.5 ± 137.8 hours (range: 1–720 hours). A possible trigger was identified in 57.5% of the patients (drug 11.7%, infection 17%, food 10.9%, or a combination of these 17.4%), while in 42.5%, no causative agent was identified. Identifying a possible trigger was associated with resolution of AU before transitioning to chronic form ($p = 0.04$, OR: 0.33 95% CI 0.12–0.92). 26.7% reported an episode of AU in the past, while 28.7% of patients reported at least one previous visit to another hospital's ED for the same episode. Complete resolution of symptoms was reported in 74.4% and 92.7% of patients 15 and 45 days after visiting the ED, respectively (mean duration 13 days ± 10). The administration of corticosteroids at the onset of the AU episode did not appear to be related to the course of the disease and the transition to CU ($p < 0.05$). In all patients with clinical symptoms and/or laboratory findings compatible with infection, the AU episode was self-limiting and did not progress to CU ($p = 0.03$, OR: 0.16, 95% CI 0.02–1.24). A

total of 7.3% (18/247) of patients with acute urticaria eventually progressed to chronic urticaria (88.9% spontaneous vs. 11.9% induced).
Conclusion: In 92.7% of patients, AU has a self-limiting course (average duration 13 days ± 10), while in 7.3%, it will turn into CU. Not identifying a causative agent, the absence of symptoms and/or laboratory findings compatible with infection are associated with an increased risk of progression to CU.
Conflicts of interest: The authors did not specify any links of interest.

000352 | Development of a mobile application to monitor prodromes and attacks of hereditary angioedema (IHAE-EPA)

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Background: Early, pre-attack signs and symptoms (prodromes), have been observed in association with Hereditary Angioedema (HAE) attacks. They are exhibited by complex manifestations, subjective and objective, enabling the patients to anticipate the attacks. Despite many reports by patients, the prodrome phenomenon is evasive and difficult to define by scientific measures. To improve the detection and assessment of HAE prodromes, a new tool, based on Patient-reported Outcome Measures (PROMS), has been recently developed. This instrument has shown its robustness in evaluating prodromes and its usefulness in predicting oncoming attacks. In the dynamic modern digital environment, an expedient personal mobile PROMS is an unmet need that can be integrated into clinical practice in the daily clinical management of HAE patients
Method: We designed and developed a mobile application (app) based on the HAE-EPA questionnaires (iHAE-EPA), capable of storing individual patient reports, analysis of data, and monitoring of clinical parameters that assist in the optimal management of HAE. The app was developed in "Flutter cross-platform" technology that can operate on both – Android and Apple iOS operating systems. The data was stored on a local server where personal and health information are securely protected. During the registration, each patient was allotted a fake ID and the data was transmitted to the protected MongoDB database. The users were able to navigate through the app pages, easily fill out the questionnaires, connect to their physician, and send their data to the server.
Results: A group of 10 physician-diagnosed HAE patients used the app successfully and were able to send real-time data to the server. Utility test was filled by the patients, rating: connectivity (100%), accessibility (97%), ease of use (97%), content visibility (97%), messaging (93%), and general satisfaction (95%). The majority of patients confirmed that the app could help them to better manage their disease and enhance communication with their physicians. Two HAE expert physicians asserted that the app was very helpful in managing and communicating with patients.
Conclusion: A new cellular disease-specific PRO instrument was developed, demonstrating high effectiveness in the management of HAE prodromes and attacks.
Conflicts of interest: The authors did not specify any links of interest.

001489 | Comparison of 150–300 mg doses of omalizumab according to efficacy and safety in patients with chronic spontaneous urticaria

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Background: Omalizumab, developed against IgE, is used in chronic spontaneous urticaria (CSU) that persists with itching and swelling despite high-dose antihistamine treatment. It is effective in CSU at doses of 150 mg or 300 mg per month. In our study, we aimed to evaluate 150 and 300 mg omalizumab doses in terms of urticaria activity score and antihistamine need in CSU patients.
Method: Retrospectively, 92 patients who were admitted to the Immunology and Allergy Diseases outpatient clinic between 2017 and 2022, who had CSU and did not respond to high-dose antihistamine therapy and received Omalizumab were included in our study. We examined whether there was significant differences between the patient groups receiving 150 mg and 300 mg omalizumab in terms of urticaria activity score, oral antihistamine need status, and the time until decaying to the non-attack stage.
Results: A total of 92 patients were included in the study. Thirty-six (39.1%) of patients receiving omalizumab were male. There were 47 (51.1%) patients receiving omalizumab 150 mg and 45 (49.9%) patients receiving omalizumab 300 mg. Both in patients receiving 150 mg or 300 mg of omalizumab, significant improvement in urticaria activity score was observed at 12 weeks from baseline (p: 0.024). When the use of antihistamine was evaluated between the patient groups using 150 mg and 300 mg omalizumab, it was observed that there was no statistically significant difference between the two groups (p: 0.664). The incidence of adverse events was the same in both groups (p: 0.516). We found that there was no significant difference between the chronic urticaria recurrence rates of both groups (p: 0.112).
Conclusion: In our study, when 150 mg and 300 mg omalizumab doses were compared in CSU patients, similar results were found in terms of quality of life, antihistamine use when needed, recurrence rate, and side effects. In this context, initially 150 mg dose may be preferred in CSU patients who need omalizumab. Patients should be reassessed for 150 or 300 mg, or discontinuation of treatment dose or after a specified period of time. However, larger population and randomized studies are needed.
Conflicts of interest: The authors did not specify any links of interest.

000445 | Serological profiling in chronic urticaria

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Background: The results on serological biomarkers as tools in diagnosing chronic urticaria (CU) are ambiguous. In this study, we aimed to identify biomarkers associated with CU diagnosis and treatment.

Method: We included 11 CU patients receiving Omalizumab (OMZ) treatment for 12 weeks and 10 healthy subjects. Samples from CU patients were collected before (BO) and after (AO) OMZ treatment. Serological biomarkers of inflammation and extracellular matrix reorganization were measured with Luminex Multiplex kits and ELISA, respectively. Extracellular vesicles (EVs) were analyzed in plasma samples by high-resolution flow cytometry and nanoparticle tracking analysis.

Results: Matrix metalloproteinase 9 (MMP9) and C-C motif chemokine 18, CCL18 concentrations were higher in CU patients in contrast to healthy (MMP9 - BO: 421 ± 197, vs. Healthy: 244 ± 69, ng/mL; CCL18 – BO: 45.8 ± 19.2 vs. Healthy: 27.8 ± 8, ng/mL). Additionally, trends of decreased concentration of collagen VI formation marker, PRO-C6, and elevated titers of CCL1 and CCL17 were found in CU compared to healthy. OMZ treatment reduced vascular endothelial growth factor (VEGF) levels in CU patients (BO: 74.7 ± 48.7 vs. AO: 63.6 ± 42.7, pg/mL) but showed no effect on MMP9. Interestingly, OMZ increased the concentration of collagen IV degradation marker, C4G (BO: 27 ± 8.1 vs. AO: 34.8 ± 9.5 ng/mL), and decreased the level of collagen I formation marker, PRO-C1 (BO: 110.1 ± 57.5 vs. AO: 74.6 ± 27 ng/mL). Moreover, higher concentrations of the macrophage activity marker, citrullinated vimentin, VICM (AO: 7.8 ± 5. vs. Healthy: 3.9 ± 1.5, ng/mL), and collagen VI degradation marker, C6M (AO: 16.4 ± 2.3 vs. Healthy: 12.2 ± 2.4, ng/mL), were observed in OMZ treated patients contrary to healthy. Concentrations of circulating EVs were comparable between the CU and healthy groups, though smaller EVs were found in CU patients. In addition, OMZ increased the concentration of $CD23^+$, $Fc\varepsilon RI^+$, and $CD36^+$ EVs, while the healthy group showed a higher level of $CD9^+CD36^+$ EVs.

Conclusion: CU was associated with elevated concentrations of chemokines (CCL1, CCL17, CCL18), vascular remodeling (MMP9) biomarkers, and the smaller EVs' population. OMZ treatment, on the other hand, was linked to changes in the homeostasis of type I, IV, and VI collagens, and to the increased activity of macrophages (VICM).

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on asthma

000979 | Farm-dust mediated asthma protection in childhood: Dendritic cell-mediated T cell priming

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Background: Asthma is one of the most prevalent chronic diseases in childhood. While prevalence is rising in western countries with high hygiene standards, children from farming areas are less affected. The so-called "protective farm effect" was replicated numerously in epidemiological studies. This study aims to identify underlying immunological mechanisms with a focus on dendritic cell (DC) mediated T cell priming.

Method: Peripheral blood mononuclear cells (PBMCs) of allergic asthmatics (AA) and healthy children (HC) were analyzed upon *in vitro* farm-dust stimulation (24h) on cellular and molecular (CyTOF data (20HC/20AA)) as well as functional level. Functional experiments comprise *inter alia* examination of (monocyte-derived(mo)) DCs (3HC/5AA) and T lymphocyte proliferation (3HC/3AA) after *in vitro* farm-dust stimulation.

Results: *In vitro* farm-dust stimulated PBMCs were demonstrated with reduced frequencies of antigen presenting cells including monocytes and DCs ($p < 0.01$) (in both phenotypes) the latter complemented by a reduced proportion of myeloid DCs (mDCs) ($p < 0.01$) with downregulated HLA-DR expression ($p < 0.05$) (CyTOF data). *In vitro* farm-dust stimulation of moDCs showed upregulated anti-inflammatory regulatory mechanism (*TNFAIP3* ($p < 0.01$)), *DUSP1* ($p < 0.05$)) and CD274 ($p < 0.05$) as well as downregulated CD209. Regarding the adaptive part of the immune system, functional investigation revealed decreased activation of effector T cells (T_{eff}) after *in vitro* farm dust stimulation for both phenotypes supplemented by reduced T cell activation and T_H2/T_H17 specific transcription factor (*GATA3*, *RORC*) expression ($p < 0.05$) exclusively in AA (CyTOF data).

Conclusion: Decreased innate antigen-presentation capacity, T_H2/T_H17 mediated immunity and T_{eff} activation as well as induction of anti-inflammatory immune regulation was demonstrated in manifest AA after *in vitro* farm-dust stimulation. These findings suggest a potential future therapeutic value of the already described asthma protective farm effect.

Conflicts of interest: Ekfsdfg.

000197 | Eosinophilic component is ubiquitous among allergic bronchopulmonary aspergillosis with atopic, non-atopic, and sans asthma – Factor analysis

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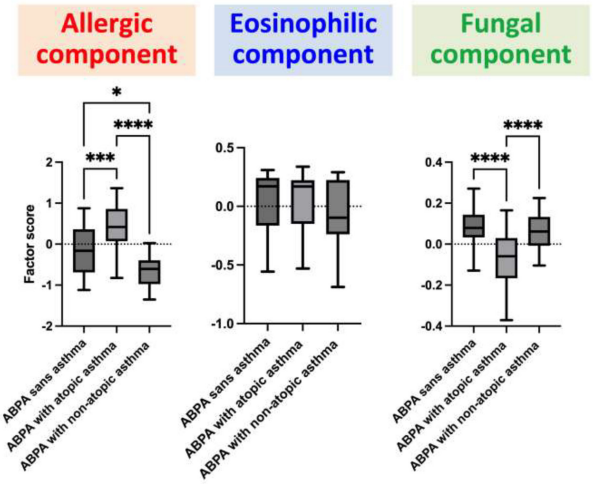
Background: Asthma is a major predisposing condition for allergic bronchopulmonary aspergillosis (ABPA). However, little is known about the impact of asthma type on the clinical characteristics of ABPA.

Method: ABPA cases satisfying Asano's criteria extracted from a prospective registry enrolled from 12 clinical centres in Japan allergic bronchopulmonary mycosis (ABPM) research program were classified into three groups according to the type of preceding asthma: ABPA sans asthma (no preceding asthma or cystic fibrosis), ABPA with atopic asthma, and ABPA with non-atopic asthma. Exploratory and confirmatory factor analyses were performed to identify the components that determined the clinical characteristics of ABPA. Patients were considered atopic if their serum IgE titer for *Dermatophagoides pteronyssinus* was ≥ 0.70 UA/L.

This work was supported by a research grant on allergic disease and immunology from the Japan Agency for Medical Research and Development (JP 22ek0410098).

Results: One hundred and eight cases satisfied Asano's criteria for ABPA, including 93 definite and 15 probable cases. Twenty-five patients (23%) had ABPA sans asthma, whereas 53 (49%) and 30 (28%) had ABPA with atopic and non-atopic asthma, respectively. Factor analysis using 14 clinical indicators identified three basic components of the clinical characteristics of ABPA: allergic, eosinophilic, and fungal components. Patients with atopic asthma showed the highest scores for the allergic component (serum levels of total and *Aspergillus fumigatus*-specific IgE and consolidation/ground glass opacity in the lungs) and the lowest scores for the fungal component (positive *A. fumigatus*-specific precipitin/IgG or positive sputum culture for *A. fumigatus*). Eosinophilic components, loaded by peripheral blood eosinophil counts, mucus plugs in bronchi, and high attenuation mucus, was consistent among the three groups.

Conclusion: The eosinophilic component of ABPA is consistent regardless of the presence of asthma or atopic predisposition and is considered a cardinal feature of ABPA.



Factor scores were compared among patients with ABPA and asthma (n = 25), ABPA with atopic asthma (n = 50), and non-atopic asthma (n = 30). * P<0.05, *** P<0.001, **** P<0.0001.

Conflicts of interest: The authors did not specify any links of interest.

000925 | The effects of allergen proteases on fibroblast-myofibroblast transition in mouse and epithelial-fibroblast co-culture model

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Background: Allergens may directly or indirectly affect airway remodeling (AR). AR is related to airway structural changes regulated by multiple factors, such as ECM accumulation, smooth muscle thickening, and myofibroblast transformation. This study aimed to investigate the effects of allergen proteases on lung remodeling and fibroblast-myofibroblast transition (FMT)

Method: We used house dust mite (HDM) induced experimental asthma models. C57BL/6J mice were challenged HDM (10 μg and 100 μg) intranasally for 2 weeks to induce mixed and neutrophilic airway inflammation, respectively. Lung lobes were collected to assess airway inflammation by histochemical staining, the number of lung fibroblasts by flow cytometry, and transcriptomic profiling by new-generation sequencing. Next, *in vitro* experiments were performed. Bronchial (BEAS-2B) and alveolar (A459) epithelial cells were maintained in ALI culture. On day 21, cells were co-cultured with airway fibroblasts (CCD-16Lu) and stimulated with allergens Der p1, p2, p6 (2–10 μg/mL) and HDM (100 μg/mL) for 48 and 72 h. Then, α-SMA and vimentin in fibroblasts were analyzed by qPCR at the mRNA level and western blot and immunofluorescence (IF) at the protein level. TGF-β was used as a positive control for FMT

Results: In the experimental asthma model, we showed asthmatic inflammation, increased mucus production, lung remodeling, and an increase in the number of lung fibroblasts in both models.

Transcriptomic profiling showed dysregulation of genes involved in abnormal ECM morphology, fibroblast function, and remodeling. *In vitro* experiments showed that all allergens, particularly the 48 h-stimulation with Der p6, increased vimentin and α-SMA gene expression in BEAS-2B/Fibroblast co-culture. According to IF analysis, HDM stimulation for 48 h increased α-SMA expression. Vimentin and α-SMA protein levels in A549/Fibroblast co-culture stimulated by HDM for 48 h were similar to that in the positive control, but only α-SMA level was statistically significant.

Conclusion: Here, we showed that stimulation with HDM and Der p6 induces FMT and can be evidence that allergen stimulation can directly affect AR. The fact that Der p1 and Der p2 did not establish the same effects may indicate that this effect varies depending on the type of allergen

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000479 | The polybacterial mucosal vaccine MV130 impairs airway inflammation in a HDM-induced eosinophilic asthma model

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Background: Asthma is a global health concern with a significant socioeconomic burden. More than half of asthma patients display a type 2 inflammation with allergic and eosinophilic pheno-endotypes. The whole heat-inactivated polybacterial preparation MV130 prevents recurrent wheezing in children and protects against experimental viral infections. Herein, we sought to investigate whether mucosal MV130 administration might dampen house dust mite (HDM)-induced eosinophilic airway inflammation.

Method: Acute HDM asthma model was developed in C57BL/6J female mice by intranasal (i.n.) HDM-sensitization on day 1 and subsequent i.n. HDM challenges on days 8–12. On days 2–4, mice were i.n. treated with MV130 or vehicle. Three days after the last HDM challenge lung function was measured and mice were sacrificed. Airway inflammation was assessed by flow cytometry and histology, and serum immunoglobulins (Igs) were quantified by ELISA. Allogeneic co-cultures of MV130-stimulated human dendritic cells (DC) and naïve $CD4^+$T cells were also performed for Treg induction evaluation.

Results: MV130 treatment significantly reduces serum total IgE, HDM-specific IgE and IgG1 and increases HDM-specific IgG2a in HDM-sensitized mice. At the local level in the lungs, MV130-treated HDM-sensitized mice show a decrease in cell recruitment with a significant reduction of inflammatory eosinophils without affecting homeostatic resident eosinophils. Likewise, the HDM-sensitized mice treated with the polybacterial vaccine display a decrease in goblet cell hyperplasia and a reduction in airway smooth muscle mass thickening, which results in less Penh and resistant index values and in consequence less bronchoconstriction. Furthermore, MV130-treated mice show a decrease in the Th2 cell response and an increase of Th1 response in the lungs compared with the HDM-sensitized mice treated with the vehicle. Interestingly, MV130 increases the capacity of human DCs to induce regulatory T cells (Tregs) and also increases that population in mice lungs. That results suggest a potential Type 2 suppressive allergen-specific Treg response which may be involved in the dampening of HDM-induced eosinophilic airway inflammation.

Conclusion: The whole-heat-polybacterial preparation MV130 prevents airway inflammation and inhibit the systemic allergic response, pointing out this vaccine as a potential asthma treatment.

Conflicts of interest: O.P. has received fee for lectures or participation in Advisory Boards from Allergy Therapeutics, Amgen, AstraZeneca, Diater, GSK, Pfizer, Inmunotek SL, Novartis, Sanofi Genzyme, Stallergenes and Regeneron. OP has received research grants from Inmunotek SL, Novartis SL, MINECO, MICINNIN and CAM. L.C. is an employee of Inmunotek SL. J.L.S. is the founder and CEO of Inmunotek SL. The rest of the authors declare no competing financial interests.

000382 | Molecular mechanism of Alt a 1-TLR4 interaction

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Background: *Alternaria alternata* is a mold with high allergic asthma-inducing capacity, mostly produced by its major allergen Alt a 1. Recent *in vitro* reports show that Alt a 1 can interact with TLR4 receptor located on the surface of macrophages to trigger immune response. However, the molecular mechanism of this interaction is still unknown. The aim of this study was to unravel the mechanism of interaction between Alt a 1 and TLR4 using different computational methodologies.

Method: Firstly, we studied the structural similarity between Alt a 1 and MD2 (the molecule responsible for presenting LPS to TLR4) using three structural alignment methods: FATCAT, CE and TM-align. We also used MMLigner to analyze the statistical inference of alignments and Procodic to study the presence of concepts. To prove if Alt a 1 could interact with TLR4, the initial geometry was obtained with blind docking calculations using ZDOCK and AlphaFold2, and the behaviour was studied by means of molecular dynamics using CHARMM3.1 force field.

Results: Results obtained in the structural alignments showed a high similarity between Alt a 1 and MD2, even without belonging to the same protein family. Therefore, we hypothesized that Alt a 1 could be simulating the role of the MD2-LPS complex. To confirm this hypothesis, different molecular dynamics simulations were carried out to study the behaviour of TLR4-MD2, TLR4-MD2-LPS and Alt a 1-TLR4 complexes over time. Focusing on the distance between the Glu586 and the Asp325 of the ectodomains (ECD) of both dimer chains, it can be observed how the distance between these residues increased in the case of the TLR4-MD2 complex, but in the case of Alt a 1-TLR4 the distance is similar to crystallographic TLR4-MD2-LPS structure. This data suggests that Alt a 1 could bound with high affinity to TLR4, in absence of MD2, promoting the dimerization of the receptor.
Conclusion: In conclusion, our *in silico* analyses support the mechanism related to Alt a 1-TLR4 interaction, showing a stable complex along simulations. Moreover, the similarity between the Alt a 1-TLR4 final complex and the TLR4-MD2-LPS structure suggests that the presence of Alt a 1 would be able to keep the C-terminal region of the ECD of TLR in close contact, allowing dimerization of the intracellular domains and the activation of the TLR pathways.
Conflicts of interest: The authors did not specify any links of interest.

000620 | PAAI – Interactive online self-learning programme for patients with asthma: A patient-and carer-centred approach on the most relevant topics to address

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*Presenting author: M. Areia

Background: Patient and Public Involvement in asthma research should focus on the engagement of patients/carers and citizens in every stage of the research cycle. However, the varying level of education and research experience may compromise this involvement, so training is recommended. In Portugal, consistent training to empower patients with asthma and their carers in health decisions or to allow them to be involved in research is not available. Our main goal is to develop and deliver a high-quality and comprehensive online educational programme for adult patients with asthma and their carers considering their needs and preferences. The initial phase presented here aims to identify the most critical topics on asthma and health research based on the educational needs of adult patients/carers with asthma and the expertise of asthma specialists.
Method: In a web-based cross-sectional study, 85 adult patients with asthma and carers, members of the ConectAR network, were asked about the topics to be addressed in the PAAI ("Programa de Auto-Aprendizagem Interativo e online para pessoas com asma") educational programme. Participants were asked to rank each topic as "very important/ important/ less important/ non-important" and to suggest additional content. Patients and carers are actively engaged in all stages of this project as co-researchers, namely in study design.
Results: A total of 37 (42%) patients/carers answered the web survey. The topics classified as "very important/ important" are ranked in Table 1, with asthma attack, living with asthma and physical activity and asthma being the ones reaching consensus. Additional topics suggested by patients/carers include Asthma in children; Social/ emotional support available for patients and carers; Experimental treatments for asthma; Biological treatments for severe asthma; Practical strategies to avoid triggers; Asthma and non-steroidal anti-inflammatory drugs; Asthma and nutrition.
Conclusion: Patients identified the most relevant topics to be included. Next, physicians and researchers will participate in a similar process, and afterwards, the most relevant topics will be set through a consensus process. By the end of the project, we anticipate having developed and implemented a high-quality, free-of-charge, online self-learning programme on asthma and health research, adapted for adult patients with asthma and their carers. This programme will

Table 1: Topics to be addressed in an educational programme on asthma, ranked by importance, based on the opinion of patients/carers (first round of Delphi).

Topics classified as "very important" / "important"	% of the participants that classified as "very important/ important"
Asthma attack (what to do during and after)	100
Living with asthma (limitations, quality of life, medication costs, mental and emotional stability, sleep)	100
Physical activity and asthma	100
How to find reliable information about asthma	97
Asthma management (symptoms, self-monitoring questionnaires, triggers)	97
Pharmacological treatment of asthma (inhaled, oral, injectable)	94
Communication doctor-patient	94
Asthma healthcare services (Public, Private)	94
Correct inhaler technic	92
Others common diseases in asthma patients	92
Non-pharmacological treatment of asthma	89
Pathophysiology of asthma (the mechanisms behind disease)	86
How to be active in asthma health research	86
Written action plan	86
Risk factors for asthma (smoking...)	83
Asthma diagnostic tests	83
Different types of asthma	83
Adherence to therapy (intentional and unintentional fails, importance)	81
Pregnancy and asthma	75

empower patients and carers to increase their knowledge about the disease and develop new skills.

Conflicts of interest: The authors did not specify any links of interest.

001404 | Feasibility of combined biological treatments with omalizumab and non-IGE-targeting monoclonal antibodies: Novel insights and a mechanism-based approach

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*Presenting author: O. Shamriz

Background: Clinical indications of omalizumab, as well as other biological treatment, are expanding. Treating physicians may encounter a dilemma regarding the safety and efficacy of co-administration of omalizumab and non-IgE-targeting agents with or without a shared immune mechanism. We aimed to present our single-center experience of combined biological treatment of omalizumab and non-IgE-targeting monoclonal antibodies

Method: This is a retrospective review of computerized medical charts of adult patients (>18 years) treated with omalizumab combined with another biological treatment in the period of January 2020 to December 2022. Patients were treated in the rheumatology and allergy and clinical immunology clinics at Hadassah Medical Center, Jerusalem, and Meir Medical Center, Kfar Saba, Israel.

Results: Our search yielded 7 patients (51–75 years; 6 females and one male) treated with omalizumab for chronic spontaneous urticaria ($n = 5$) and asthma ($n = 2$). In addition, the patients were treated with co-administered biologics inhibiting the function of interleukin (IL)-5 (mepolizumab, and benralizumab; $n = 1$, each), IL-17A (Secukinumab; $n = 1$), IL-4/13 (dupilumab; $n = 1$), IL-1 (anakinra; $n = 1$), Calcitonin Gene-related Peptide (CGRP; $n = 1$) and Tumor Necrosis Factor (TNF)-α (etanercept; $n = 1$). Dual biotherapy was adninistered for 9–34 months with a subsequent reduction in immunosuppressive treatment and clinical resolution of symptoms in all of the patients. None of the patients had adverse events related to the combined biological treatment.

Conclusion: Combined biological treatments with omalizumab and non-IgE-targeting monoclonal antibodies are safe and effective. Discontinuation of non-IgE targeting agents in patients treated with omalizumab should be discouraged.

Conflicts of interest: The authors did not specify any links of interest.

000628 | Reduction of systemic corticosteroid courses in severe asthmatic patients receiving a biological treatment

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Background: Short and long-term secondary effects of treatment with systemic corticosteroids (SCS) for controlling asthma exacerbations, even short courses, are common. Currently, the use of biological drugs in the upper steps of different clinical practice guidelines is recommended for the management of difficult-to-control asthma. Total number of annual courses of SCS has been proposed as an indicator of the efficiency of these treatments.

Method: A retrospective study of patients followed up in our hospital with severe asthma was carried out.

Epidemiological data, evolution records and the number of SCS courses were registered. The period investigated was from 2013 until the end of 2022. Information of the two years' period prior starting the biological treatment was specially assessed. The patients included were treated with omalizumab, mepolizumab or reslizumab. The relative risk reduction (RRR) value of each of the 3 biologics was estimatedand compared among them.

Results: Thirteen patients were on treatment with omalizumab (70% women, mean age 51 years [range 19–81] and their treatment duration mean was 6.8 years [4–8]). Seventeen patients were on treatment with mepolizumab (65% women, mean age 56 years [40–79] and their treatment duration mean was 5.6 years [2–5]). Five patients were on treatment with reslizumab (80% women, mean age 56 years [39–75] and their treatment duration mean was 3 years [4–1]). Calculation of RRR values for the different groups were: 71% (95% CI 55–80%), 72% (65–76%), and 64% (44–85%) for omalizumab, mepolizumab, and reslizumab, respectively. The statistical analysis of the risk differences comparison showed no statistical differences among them.

Conclusion: Add-on biological therapeutics, is closely related to a better control of the disease in patients with severe asthma. Our experience confirms that omalizumab, mepolizumab and reslizumab, do reduce the use of SCS cycles as rescue treatment for asthmatic exacerbations.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on pediatric allergy

000028 | Early enhanced treatment for infant atopic dermatitis prevents food allergy: A multicenter, parallel-group, open-label, assessor-blind, randomized controlled trial (PACI study)

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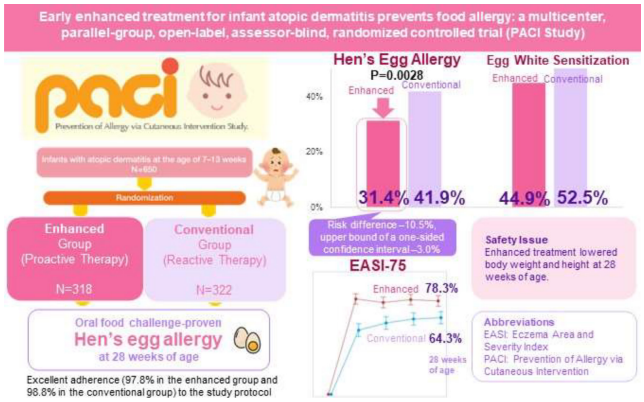
*Presenting author: K. Yamamoto-Hanada

Background: Early-onset atopic dermatitis (AD) increases the risk of food allergy, suggesting that transcutaneous sensitization may occur through inflamed skin. We tested whether enhanced treatment of atopic dermatitis during infancy can prevent the onset of food allergy.

Method: Infants aged 7–13 weeks with AD were randomly assigned to enhanced proactive or conventional reactive treatment. The primary outcome was the proportion with immediate hen's egg allergy confirmed by oral food challenge at 28 weeks of age.

Results: 650 infants were randomly assigned, and 640 infants (enhanced [$n = 318$] or conventional [$n = 322$] treatment) were analyzed. Hen's egg allergy was lower in the enhanced group than in the conventional group(31.4% vs. 41.9%, $p = 0.0028$; risk difference −10.5%, upper bound of a one-sided confidence interval [CI] −3.0%). Hen's egg white IgE sensitization was also lower in the enhanced group (44.9% vs. 52.5%; risk difference −7.6%, 95%CI −15.4% to 0.2%). Although AD severity was reduced in the enhanced treatment group (EASI-75 and 90 at 28 weeks of age was 78.3 %, and 64.9 % compared with 64.3 %, and 50.5 % in the conventional group), body weight (mean difference −422 g, 95%CI −553 g to −292 g) and body height (mean difference −0.8 cm, 95%CI −1.22 cm to −0.33 cm) at 28 weeks of age was lower in the enhanced group.

Conclusion: Enhanced proactive treatment for infant atopic dermatitis reduces the risk of hen's egg allergy with better atopic dermatitis control. But at the expense of reduced body weight and height at 28 weeks. Modified proactive treatment to minimize adverse effects of TCSs should be considered in further studies.



Conflicts of interest: The authors did not specify any links of interest.

000450 | Diet diversity in pregnancy and early allergic manifestations in the offspring

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Background: It is important to disentangle the multifactorial ethiology behind allergic diseases for which increasing incidences are evident. Maternal diet is suggested to be one determinant of early life allergy prevention since it may influence on the neonatal innate and adaptive immune system. The aim of this study was to investigate if a diverse diet during pregnancy is associated with subsequent decreased risk of early allergic manifestations in the offspring.

Method: We utilized a diet diversity (DD) score including 40 food items or groups (presented in Table 1), based on the present dietary guidelines in Sweden, in 3200 pregnant women from the population-based prospective NorthPop Birth Cohort Study. Associations to

the cumulative incidence of eczema, wheeze, physician diagnosed asthma, and physician diagnosed food allergy in the first 18 months of life in the offspring were assessed using multivariable logistic regression models, presenting odds ratios (ORs) per 1 unit increase and per quartile in DD-score. For severity of eczema according to Patient Oriented Eczema Measure (POEM)-score), multinominal logistic regression models were used. Screening for senzitization to food and inhalant allergens was performed at 18 months of age in 1922 of the study participants.

Results: Higher diet diversity scores in pregnancy were associated with a decreased risk of physician diagnosed food allergy until 18 months age in the fully adjusted model, OR per 1 unit increase in DD-score Model 3: 0.96, 95% CI 0.92–1.00, P 0.038 (Fig 1), and for quartile 4 of DD-score, the OR was 0.58, 95% CI 0.32–0.95 compared to quartile 1. There was an indication of an association between energy adjusted DD-scores and infant wheeze (0.97, 0.96–0.99, *p* 0.009) but it did not remain significant after further adjustments. No associations were found between high gestational diet diversity and decreased offspring eczema or asthma risk or to sensitization status at 18 months of age in multivariable models.

Conclusion: A more diverse diet in pregnancy may reduce the risk of food allergy in early life and could be a promising strategy to reduce early childhood food allergy incidence and its associated individual and healthcare burden. More work is needed to elaborate robust measures of maternal diet diversity to disentangle its impact on early overall allergy risk.

Table 1. Included food items (n=40) in the Dietary Diversity (DD) score in pregnant women in the Swedish NorthPop Birth Cohort Study. The DD score was adjusted for total energy intake using the residual method.

	Foods	Cutoff frequency or other measure		Foods	Cutoff frequency or other measure
	Fiber rich foods:			**Fruits & berries**	
1	Fiber cereals	≥1-3 t/w = 1p	2	All fruits	1-2 t/day =1p
2	Fiber porridge	≥1-3 t/w = 1p	2	All berries	≥1-3 t/w = 1p
				Meat	
3	Fiber pasta	≥1-3 t/w = 1p	2	Red meat	1-3 t/w to 4-6 t/w
4	Brown rice	≥1-3 t/w = 1p	2	White meat	1-3 t/w to 4-6 t/w
5	Bulgur/couscous/grains	≥1-3 t/w = 1p		**Fish & seafood**	
	Fiber rich bread		2	Fatty fish	≥1-3 t/w = 1p
6	Fiber rich soft bread[a]	If most common bread=1p[a]	2	Lean fish	≥1-3 t/w = 1p
7	Fiber rich crisp bread[a]	If most common bread=1p[a]	3	Sea food	≥1-3 t/w = 1p
8	Boiled potatoes	≥1-3 t/w = 1p	3	**Egg**	≥1-3 t/w = 1p
9	Carrots	≥1-3 t/w = 1p	3	**Pulses**	≥1-3 t/w = 1p
10	Root vegetables	≥1-3 t/w = 1p	3	**Soya bean products**	≥1-3 t/w = 1p
	Cabbage			**Dairy products**	
11	Cauliflower	≥1-3 t/w = 1p	3	Unpasteurized milk	If yes =1p
12	Broccoli	≥1-3 t/w = 1p	3	Cow's milk	≥2 dl/day = 1p
13	White cabbage	≥1-3 t/w = 1p	3	Milk replacement	≥2 dl/day = 1p
	Green vegetables		3	Soured milk unsweetened	≥1-3 t/w = 1p
14	Lettuce	≥1-3 t/w = 1p	3	Yoghurt unsweetened	≥1-3 t/w = 1p
15	Avocado	≥1-3 t/w = 1p	3	Quark/cottage cheese	≥1-3 t/w = 1p
16	Cucumber	≥1-3 t/w = 1p	4	**Nuts, all**	≥1-3 t/w = 1p
	Other vegetables			**→ DD-score**	**Min 0p, Max 40p**
17	Frozen vegetables	≥1-3 t/w = 1p			
18	Sweet pepper	≥1-3 t/w = 1p			
19	Tomatoes	≥1-3 t/w = 1p			
20	Corn	≥1-3 t/w = 1p			
21	Onion	≥1-3 t/w = 1p			
22	Garlic	≥1-3 t/w = 1p			
23	Mushroom	≥1-3 t/w = 1p			

[a] If ranked as the most common type of consumed bread (1 or 2 on a ranking scale of maximum 6) = 1p
Abbreviations: t/w, times/week; p, points; DD, diet diversity

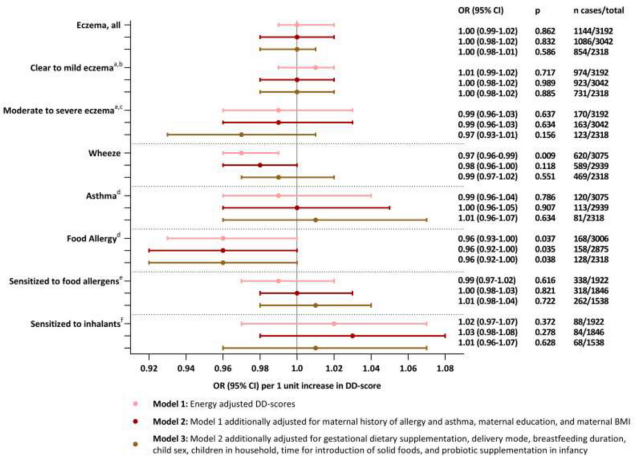

Figure 1. Association between diet diversity (DD) score in pregnancy and cumulative incidence of allergic manifestations until the age of 18 months (n=3200). Colored dots represent the odds ratio (OR) per 1 unit increase in DD-score and colored lines represents the 95% confidence intervals.

[a] ORs produced with multinominal logistic regression with 'no eczema' as reference
[b] According to POEM-score 0-7
[c] According to POEM-score 8-28
[d] Physician diagnosed
[e] Sensitized to food mix (fx5) with cow's milk, egg white, wheat, peanuts, soy, and cod. Sensitization was defined as positive if IgE levels ≥ 0.35 kU/L.
[f] Sensitized to inhalation mix (Phadiatop) for the allergen allergens birch, timothy, mug wort, cat, dog, horse, *Cladosporium herbarum, Dermatophagoides pteronyssinus* and *farina*. Sensitization was defined as positive if IgE levels ≥ 0.35 kU/L.
POEM, Patient Oriented Eczema Measure

Conflicts of interest: The authors did not specify any links of interest.

000828 | Plasma levels of polyunsaturated fatty acids in childhood and adolescence in relation to rhinitis and allergic sensitization up to adulthood

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Background: Nutritional factors, including very long-chain (VLC) polyunsaturated fatty acids (PUFA), have been suggested to influence the risk of allergic disease including rhinitis and allergic sensitization. Plasma levels of VLC PUFA have been shown to be valid biomarkers of dietary intake. The aim of the study was to investigate the role of omega-3 (n-3) and omega-6 (n-6) PUFA in plasma phospholipids in childhood and adolescence for the development of rhinitis and allergic sensitization up to young adulthood.

Method: This study included participants from the Swedish birth cohort BAMSE (*n* = 825). Proportions of fatty acids in plasma

phospholipids (α-linolenic acid [18:3n−3], the sum of VLC n−3 PUFAs: eicosapentaenoic acid [20:5n−3], docosahexaenoic acid [22:6n−3], and docosapentaenoic acid [22:5n−3]; and the n−6 PUFAs linoleic acid [18:2n−6] and arachidonic acid [AA; 20:4n−6]) were analyzed at 8 years and 16 years using gas chromatography. Rhinitis was defined based on questionnaires. Allergic sensitization was defined as allergen-specific IgE antibodies (≥0.35 kU_A/L) against Phadiatop at 8, 16 and 24 years. Each PUFA was dichotomized into high or low based on the median at 8 and 16 years and analyzed in relation to rhinitis with and without allergic sensitization at 24 years by logistic regression. Longitudinal analyses of rhinitis and allergic sensitization from 8–24 years were performed by generalized estimating equations.

Results: The prevalence of rhinitis increased from 16.2% at 8 years to 32.0% at 24 years, while the prevalence of allergic sensitization to airborne allergens increased from 28.6% to 46.0%. High plasma proportions of VLC n-3 PUFA as well as AA at age 8 years were inversely associated with prevalent rhinitis at 24 years (OR 0.70, 95% CI 0.52, 0.95 and OR 0.65, 95% CI 0.48, 0.88, respectively). These associations were observed for rhinitis with, but not without allergic sensitization. High plasma proportions of VLC n-3 PUFA as well as AA were further associated with a decreased risk of allergic sensitization longitudinally up to 24 years (OR 0.81, 95% CI 0.71, 0.91 and OR 0.85, 95% CI 0.75, 0.97, respectively).

Conclusion: Results from this population-based prospective cohort with repeatedly measured biomarkers of dietary PUFA intake suggest that high plasma proportions of VLC n-3 and certain n-6 PUFA in childhood is associated with decreased risk of rhinitis and allergic sensitization up to young adulthood.

Conflicts of interest: MvH has received lecture fee from Thermo Fisher outside the submitted work.

000425 | Earlier and more frequent consumption of allergenic foods among infants after the update of Swedish guidelines on complementary feeding

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*Presenting author: J. Österlund

Background: Studies have reported that early introduction of allergenic foods, such as peanuts and egg, can reduce the risk of food allergies in high-risk children. Many international guidelines recommend introduction in the first year of life. In June 2019 the Swedish National Food agency released updated guidelines but the population response is still unknown. We aimed to examine if age at introduction and consumption frequency of allergenic foods have changed since the release of updated national guidelines on the introduction of solid foods in Sweden.

Method: Children born between June 2016 and December 2018 were compared to children born between June 2019 and April 2021 using data from the longitudinal population-based birth cohort NorthPop. A total of 3686 infants were included in the study. Data on food introduction were prospectively collected using web-based questionnaires. The primary outcome was introduction of egg, fish, legumes, soy protein, peanuts, almond, cashew nut, hazelnut, walnut and Brazil nut before 11 months of age. The secondary outcome was the consumption frequency of egg, fish, legumes, peanuts, almond, cashew nut, hazelnut, walnut, Brazil nut the month prior to completing the 9-month-questionnaire. Multiple imputation was applied to handle missing values. The primary outcome was analyzed using simple and multivariable logistic regression with results expressed as adjusted odds ratios (aORs). The secondary outcome was analyzed using ordinal logistic regression and expressed as adjusted odds ratios with the same confounders as for the primary outcome.

Results: The proportion of infants who had introduced egg, legumes, soy protein, peanuts, cashew nut and almonds in their diet during the first year of life increased after the release of updated national guidelines. The most significant change was seen for legumes (55.2% to 69.8% aOR 1.90 (95% CI: 1.62 to 2.24) and peanuts (29.2% to 43.2% aOR 1.87 (95% CI: 1.55 to 2.24). The consumption frequency also increased for egg, legumes, peanuts, cashew nut and almonds.

Conclusion: Since the release of updated guidelines, infants in the study population now introduce egg, legumes, soy protein, peanuts, cashew nut and almonds earlier and consume egg, legumes, peanuts, cashew nut and almonds more frequently than before.

	Previous guidelines	New guidelines			
Introduction before 9-11 months	N (%)*	N (%) **	χ^2 (P-value)	OR (95% CI)	aOR (95% CI)
Egg introduction			**<0.001**	**1.647 (1.330-2.039)**	**1.661 (1.340-2.060)**
Introduced	1173 (82.3)	1149 (88.7)			
Not introduced	252 (17.7)	146 (11.3)			
Fish introduction			0.762	1.052 (0.729-1.519)	1.057 (0.726-1.539)
Introduced	1369 (96.1)	1247 (96.3)			
Not introduced	56 (3.9)	48 (3.7)			
Legume introduction			**<0.001**	**1.918 (1.642-2.240)**	**1.902 (1.617-2.238)**
Introduced	545 (55.2)	904 (69.8)			
Not introduced	442 (44.8)	391 (30.2)			
Soy introduction			**0.009**	**1.328 (1.047-1.685)**	**1.309 (1.025-1.671)**
Introduced	192 (19.5)	311 (24.0)			
Not introduced	795 (80.5)	984 (76.0)			
Peanut introduction			**<0.001**	**1.858 (1.552-2.225)**	**1.865 (1.551-2.243)**
Introduced	416 (29.2)	560 (43.2)			
Not introduced	1009 (70.8)	735 (56.8)			
Almond introduction			**0.003**	**1.422 (1.129-1.790)**	**1.399 (1.111-1.762)**
Introduced	167 (11.7)	203 (15.7)			
Not introduced	158 (88.3)	1092 (84.3)			
Cashew introduction			**0.047**	**1.322 (1.031-1.694)**	**1.319 (1.026-1.696)**
Introduced	133 (9.3)	151 (11.7)			
Not introduced	1292 (90.7	1144 (88.3)			
Hazelnut introduction			0.413	1.190 (0.858-1.650)	1.149 (0.823-1.604)
Introduced	89 (6.2)	91 (7.0)			
Not introduced	1336 (93.8)	1204 (93.0)			
Walnut introduction			**0.039**	**1.435 (1.033-1.992)**	1.390 (0.993-1.946)
Introduced	79 (5.5)	97 (7.5)			
Not introduced	1346 (94.5)	1198 (92.5)			
Brazil nut introduction			0.525	0.881 (0.415-1.867)	N/A
Introduced	18 (1.3)	13 (1.0)			
Not introduced	1407 (98.7)	1282 (99.0)			

Introduction of solid foods at 9-11 months and comparison between the two time periods in relation to the new guidelines. Significant differences in bold. OR- Odds ratio, aOR – Adjusted odds ratio. Odds ratio for comparison between the new guidelines to the previous guidelines.
**Missing data for age of introduction for egg, fish, almond, peanut, almond, cashew, hazelnut, brazil nut (N=500 [26.0%]) and for soy and legume (N=938 [48.7%]) due to the question first added to the questionnaire in March 2018*
*** Missing data for all foods (n=466 [26.5%])*

Conflicts of interest: Christina West has received research funding, which was paid directly to the institution, from Thermo Fisher Scientific/Phadia and Arla Foods.

001364 | Nasal interferon-swap in wheezing and asthmatic children carrying 17q21 risk allel

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Background: The susceptibility locus on chromosome 17q21 represents the best validated genetic risk factor for childhood-onset asthma. To elucidate the urgently-needed functional relationship between 17q21-encoded genes and the resulting pathogenic processes in the airway mucosa, we examined the nasal transcriptome of healthy, wheezing, and asthmatic children regarding their 17q21 variants.

Method: We analyzed the nasal transcriptome from nasal brushes of 48 healthy, 36 wheezing and 110 asthmatic children in relation to their genetic aberrations at the 17q21 locus using whole-genome microarrays for low-input rare samples. From a subset of these children nasal secretions were collected and IFN-protein levels were determined.

Results: This study demonstrates that the mutated 17q21 locus in unaffected, healthy children leads to a broad alteration in local gene expression signature, including loss of an immunocompetent, homeostatic signature of the nasal epithelium. These changes largely were associated with *GSDMB* enrichment in both disease entities. We visualized the immunological impact of elevated nasal *GSDMB* expression intensity and identified a type-1 pro-inflammatory, cell-lytic immune signature involving key genes such as *IFNG*, *CD8A*, *GZMA* and *FASL*. Surprisingly, 17q21 risk allele carriers lack class-I and class-III interferon response as well as show a deficit in interferon receptor expression suggesting an IFN deafness possibly caused by chronic IFN-γ exposure.

Conclusion: In conclusion, this study demonstrates that 17q21 risk allele causes a *GSDMB*-associated drop in airway immune competence. The data illustrate that *GSDMB* mediates a novel mechanism triggering a nasal cell-lytic $CD8^+$ response accompanied by an IFN swap from class-I/-III to class II.

Conflicts of interest: The authors did not specify any links of interest.

000826 | New onset allergy after heart transplant in children

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Background: It is known that there is a higher rate of allergies and other immune manifestations among patients that have received a solid organ transplant, affecting a variety of organs and systems and, thus, requiring a multidisciplinary approach. The cause of these phenomena is thought to be multifactorial including the immunosuppressant therapy, age at the time of the transplant, early thymectomy, type of organ involved, etc.

Method: Our aim was to describe the diversity of new onset allergy manifestations in a group of children who underwent a heart transplant.

We conducted a cross sectional study of patients, under 18 years old, who underwent heart transplantation from 2009 to 2021, through an evaluation of the medical records. These patients are regularly followed by a group of physicians formed by allergists, immunologists, dermatologists, cardiologists and gastroenterologists.

Results: 99 children received a heart transplant between 2009–2021. There were 12 cases of new onset allergy, 11 males, with a cumulative incidence of 12.12%. The median age of transplant was of 0.4 (0.3–1.55) years and 1.75 (0.95–2) years between the initiation of tacrolimus and the onset of allergy symptoms, all but one received tacrolimus since the procedure. The levels of IgE and eosinophils were of 987 (164–4545)KU/L and 0.35 (0.05–0.5)E3/µL respectively. Food allergy was the main cause of allergy, being fish (7/11), egg (6/11), nuts (6/11) and legumes (5/11) the most common allergens, all having facial angioedema as the principal manifestation only being accompanied by urticaria in 2 cases and 5/11 children having at least one anaphylactic reaction. As to other allergic manifestations we encountered eosinophilic esophagitis in 5/12 cases, 3/12 children had drug hypersensitivity, 3/12 were asthmatics and 3/12 had rhino conjunctivitis. There were, also, 7 children with atopic dermatitis and 7 with cheilitis.

Conclusion: The onset of a new allergy in children with a history of heart transplant is an important cause of morbidity with a high number of food allergies with facial angioedema as the principal form of manifestation and a significant rate of anaphylaxis and eosinophil-associated gastrointestinal disorders. It is, also, notable the rate of eczema and cheilitis, showed by almost half of the patients. These alterations are, probably, due to an imbalance of the Th1/Th2 response that needs to be furthered studied though what is very clear is the necessity of multidisciplinary management of these patients.

Conflicts of interest: The authors did not specify any links of interest.

001068 | Respiratory allergic manifestations (asthma and rhinitis) in children followed for food allergy

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Background: Association between respiratory and food allergies is well-known, but only few studies have analyzed the prevalence of respiratory diseases in children admitted for an oral food challenge (OFC).

Method: Our objective was to evaluate the prevalence of asthma and allergic rhinitis among children admitted for OFC. Our secondary objectives were to evaluate our professional practices regarding the exploration of respiratory symptoms and to evaluate the association between respiratory diseases and food allergy outcomes.

We retrospectively analyzed medical files of children, who were admitted for an OFC in the Allergy Pediatric Unit of the University Hospital of Nancy over 2 years (2020–2021). We collected the presence of respiratory diseases and evaluated their association with food allergy phenotypes.

Results: Among the 790 children included, mean age at data collection was 8.7 ±4.7 SD years old (yo). The age at diagnosis of food allergy was mainly between 0–2 yo (68.9%) and 3–5 yo (22.7%); 68% were polysensitized. Diagnostic of asthma was confirmed or suspected in 388 patients (49.1%) and allergic rhinitis for 383 patients (48.5%) but data were missing respectively in 18.1% and 30.8%. Previous hospitalization for asthma was reported in 60 children (7.6%), including 3 patients in intensive care unit. Asthma was significantly associated with food allergy to tree nuts ($p < 0.01$), peanuts ($p < 0.001$), legumes ($p < 0.001$) and wheat/gluten ($p < 0.01$) but not to egg or milk. Asthma was significantly associated with history of grade 3 reaction according to the Ring & Messmer classification ($p < 0.0001$), and confirmed food allergy during OFC ($p < 0.0001$).

Conclusion: Half of patients admitted for an OFC also have asthma or allergic rhinitis, but the search for these comorbidities is too often missing, especially for allergic rhinitis. Asthma was associated with food allergies known to be more persistent and with an increased prevalence of history of severe anaphylaxis.

Conflicts of interest: The authors did not specify any links of interest.

000064 | The milk ladder for IgE-mediated cow's milk protein allergy in Ireland: A ten-year retrospective analysis

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Background: Cow's milk protein allergy (CMPA) is one of the most common food allergies in infancy and childhood. In Ireland, CMPA affects approximately 1% of infants. Disease duration varies between individuals and prolonged sensitisation to cow's milk places patients at increased risk of anaphylaxis due to accidental exposure to milk.

Studies however have shown that there is a good response to the introduction of baked milk products in those with CMPA. Milk proteins change with exposure to heat, thus altering its degree of allergenicity, making this method especially favourable with good results. This can be achieved by the use of ladders, progressing in a stepwise manner from milk proteins that are the most broken down to eventually introducing the raw product. The Milk ladder was adopted as a method of milk introduction for IgE-mediated CMPA in Ireland in 2011.

Aim: to assess the introduction of milk in IgE-mediated CMPA using the home introduction milk ladder strategy (IMAP 12) in children with IgE-mediated CMPA in Ireland.

Method: A retrospective chart review of 200 patients diagnosed with IgE-mediated CMPA attending the paediatric allergy clinic between 2011 and 2020 was conducted. An adapted Milk Allergy in Primary care (MAP) Guideline, also known as the milk ladder was used. This ladder uses a 12-step guideline for the reintroduction of different food containing different amounts of milk protein. The ladder introduces the smallest amount of the allergen first and progressing to more as the child tolerates it, thus progressing up the ladder and increasing his/her exposure to the proteins over time.

The main outcome was the introduction of cow's milk proteins, defined as the intake of more than 150 ml of cow's milk or the equivalent intake of 4.5 g milk protein daily without any symptomatology. Secondary outcomes included skin prick test wheal size and milk specific IgE at diagnosis, history of other atopic conditions, and allergic symptoms experienced while on the milk ladder.

Results: The proportion of success in the milk ladder group was 148 patients (86.6%) (95% confidence interval (CI): 80.6–90.9). The number of clinical visits were 2–4 with a median of 2 and the duration of treatment varied between 8–23 months with a median of 12.5 months.

The number of accidental exposures to milk was recorded in 32 patients (18.7%; 95% CI 13.6–25.2) and number patients who had

anaphylactic reactions were 3 (1.8%; 95% CI 06–5.0), none of which we caused from the milk ladder management.

A higher value of Skin Prick Test was not associated with failure to complete the milk ladder. A higher value of whole milk specific IgE was associated with a failure of the introduction ($p < 0.01$). There was no difference in progression through the milk ladder in children with concomitant atopic conditions or food allergies compared to children with no concomitant conditions.

Conclusion: The use of the milk ladder in CMPA patients is a safe and effective method of introducing milk. Future research should compare the effectiveness of the milk ladder to other CMPA treatments, and a prospective cohort study is also recommended to further establish the milk ladder as an effective CMPA treatment.

Conflicts of interest: The authors did not specify any links of interest.

001631 | Tolerance "in real life" to tuna as first assessment in pediatric population with fish allergy. predictive biomarkers

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Background: To evaluate tolerance to canned tuna (C-tuna) and fresh tuna (F-tuna) in children with fish allergy as a first assessment in oral food challenge (OFC) and follow up tolerance at home. To study possible reactivity biomarkers.

Method: Prospective study in children with fish allergy [clinical suspicion, positive skin prick test (SPT) and positive specific-IgE (s-IgE)] between 2014–2020. S-IgE, s-IgE/total IgE(t-IgE), Gad-C1-sIgE, Gad-C1-sIgE /t-IgE were performed 6 months before OFC. OFC accumulative dose >12 years: 34g protein; <12 years: 22g. Follow up telephone calls to assess tolerance at home.

Results: 145 patients. 96.5% sensitization to multiple fish species. OFC performed: C-tuna 140, F-tuna 120. Age 8 years (1–17). Median Gad-C1-sIgE 3.69KUI/L (0.9–10.8), Gad-C1-sIgE/t-IgE 0.65 (0.2–1.81); median tuna-sIgE 2.12KUI/L (0.7–7.29), median tuna-sIgE/t-IgE 0.4.

Tolerance in OFC: C-tuna 97% (136). Reactions: grade-1 50% (2), grade-2 50% (2). F-tuna 84.2% (101). Reactions: grade-1 28% (5), grade-2 44.4% (8), grade-3 16.7% (3), grade-4 11.1% (2).

A statistically significant association was found between Gad-C1-sIgE levels and tolerance to F-tuna. Median in non-tolerant group was 5.65, compared to 2.68 in the tolerant group ($p = 0.015$). ROC curves: F-tuna AUC 0.76, Gad-C1-sIgE 4.48 KUI/L (S75%, E70%).

Adverse events at home: C-tuna 5.8% (8); grade-1 75% (6), grade-2 25% (2). F-tuna 28.7% (29); grade-1 71.4%, grade-2 14.2%, grade-4 14.2%. C-tuna and F-tuna were introduced in 91% and 60% respectively into their diet.

Gad-C1-sIgE value of 8.89 KUI/L predicts home C-Tuna tolerance (AUC = 0.77; accuracy = 81%, sensitivity = 75%, specificity = 82%). Other comparisons found no association with tolerance at home.

Conclusion: C-tuna and F-tuna tolerance at OFC is high, but there is a significant percentage of adverse events at home, with a final tolerance of 91% and 60% respectively.

Most reactions at home are mild, however, there may be anaphylaxis. Patient follow up and home reactions advice is important.

Gad-C1-sIgE ≤ 4.48 KUI/L is a positive predictive value for F-tuna tolerance at OFC while there's not an optimal biomarker for future F-tuna home tolerance.

Gad-C1-sIgE > 8.89 KUI/L may help predict reactions at home to C-tuna.

Conflicts of interest: The authors did not specify any links of interest.

000079 | Longitudinal associations between behaviour concerning UV-light exposure and susceptibility to allergies in early childhood

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*Presenting author: K. Rueter

Background: Allergy is the most common and earliest manifestation of the vulnerability of the immune system to modern environmental and lifestyle change. 30–40% of the world's population is affected by at least one allergic disease. While multifactorial, a consistent allergy risk factor has been reduced UV-light exposure. However, vitamin D supplementation studies have been disappointing, raising the question whether independent effects of UV-light exposure may play a role. This is the first study to investigate longitudinally whether UV-light exposure and sun protective behaviours influence the development of early childhood allergic disease.

Method: Data on outdoor/sunlight exposure, sun protective behaviours, skin type and vitamin D levels were collected. Children ($n = 195$) were assessd for allergic disease outcomes at 3, 6, 12, and 30 months. Using generalized-mixed-models we investigated changes over the four time points for any allergic disease outcomes and specifically eczema, food allergy, wheeze or sensitisation. Fixed effects for confounding variables were examined in unadjusted models.

Results: Focussing on any allergic disease development, protective fixed effects were found for outdoor daily sun exposure time

(F = 32.0; OR 0.98; CI 0.98–0.99; $p < 0.001$) and sunscreen use (F = 9.51; $p < 0.001$). Individual eczema outcome model reported that children who sometimes wore sunscreen were at increased risk of eczema development (OR 0.50; CI 0.28–0.89; $p = 0.02$). Wheeze models showed protective fixed effects for season of birth (F = 3.35; $p = 0.02$) with a decreased risk for children born in autumn (OR = 0.39; CI 0.20–0.75; $p = 0.005$), time spent outdoors (F = 9.1; OR = 1.00; CI 0.99–1.00; $p = 0.003$) and increased daily sun exposure (F = 8.1; OR 0.91; CI 0.86–0.97; $p = 0.004$). No effects were detected for vitamin D levels/supplementation, skin type or exposure.

Conclusion: Longitudinally our data shows a protective link between time spent outdoors/in the sun and any allergic disease outcomes, specifically wheeze outcomes. Observational studies have described an inverse association between vitamin D status and allergic disease. However, none of these previous studies evaluated UV-light exposure in addition to vitamin D status. Our results suggest that vitamin D independent UV-light induced effects may be responsible for these associations. Larger, well designed studies are required to explore the role of UV light exposure on allergy outcomes outweighing potential benefits and cancer risks.

Conflicts of interest: The authors did not specify any links of interest.

000480 | Routines, knowledge and safety among pre-school and school personnel regarding preventing and managing allergies in children

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Background: Allergic diseases are common in children and may manifest for the first time at school. They may impair school performance, reduce quality of life, and cause severe reactions. However, less is known about how to manage allergies at school. The aim of this survey was to assess routines, level of knowledge and safety/concern among pre-school and school personnel when working with children with allergies.

Method: A web-based questionnaire was administered to personnel from 42 pre-schools ($n = 362$) and 30 schools ($n = 657$) in Stockholm Region from September 2021 to September 2022. Descriptive data on routines, knowledge and safety are presented as percentages (%). In addition, using ten-point Likert scales, the results were grouped into low (1–4), medium (5–8), and high/good (9–10) response categories. Differences between pre-school and school personnel results were tested by multinomial logistic regression, considering school clustering.

Results: Out of 1,019 respondents, 36% worked in pre-schools and 64% in schools. In total, routines regarding how to take care of children with allergies, how to act in the event of an allergic reaction, and how to manage special diets for children with food allergies were in place in 78%, 73% and 87% of respondents, respectively. Routines worked well in 50% regarding how to take care of allergic children, in 45% how to act in the event of an allergic reaction, and in 63% how to manage special diets. Less than 33% had a good level of knowledge about food allergy, allergy to pets, pollen, eczema, asthma and rhinitis, 21% had a good level of knowledge of how to take care of a child who has an allergic reaction, and 41% how to manage special diets for children with food allergies. Less than 30% had a high sense of security/safety when meeting/taking care of allergic children. Additionally, about one out of six respondents reported high anxiety about children getting allergic reactions or children with food allergies getting unappropriate food. Pre-school personnel were more likely to have routines in place, and reported that these worked well, in comparison to school personnel ($p < 0.05$).

Conclusion: Routines regarding children with allergies are available for pre-school/school personnel. However, how routines work, as well as level of knowledge and safety need to be improved. Such an improvement may reduce anxiety and improve care, hence children with allergies will obtain the same conditions and development as their peers.

Conflicts of interest: The authors did not specify any links of interest.

000813 | Patterns of early childhood allergy prevention behaviours: Results of the KUNO-Kids health study

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Background: Early childhood allergy prevention (ECAP) practices include parental behaviours related to exposure to or avoidance of potential allergens in the child. The S3 guideline in Germany specifies not only the behaviours recommended for allergy prevention, but also discourages most measures related to avoidance of allergens. This study aimed to identify patterns of ECAP behaviours practiced in German families.

Method: 1662 mothers participating in the KUNO-Kids health study in the area of Regensburg, Germany were surveyed at birth of child, and after 1, 6, and 12 months using interviews and self-report questionnaires on several ECAP behaviours including nutrition and the living environment. Latent class analysis was used to analyse patterns of ECAP behaviours. Models with different numbers of classes were compared using the Bayesian information criterion (BIC) as a criterion for model selection.

Results: A model with three classes showed the best fit (BIC = 16967.8). Classes were comparable regarding fish consumption in pregnancy

and the child's diet, timing of introduction of solid foods and feeding farm milk. The most prominent characteristic of class one (52.29%) was exclusively breastfeeding for at least 4 months. The other two classes were characterised by greater probabilities of exclusive breastfeeding for less than 4 months or not at all. Most notably, class two (18.57%) comprised mothers who fed hypoallergenic infant milk, who avoided specific foods in the child's diet and who implemented measures against house dust mites. Class three (27.52%) was characterised by a higher probability of exposing the child to tobacco smoke.

Conclusion: This study investigated a range of parental ECAP behaviours, including both recommended and not recommended behaviours, using data from a large and well characterized birth cohort in Germany. We identified different patterns of ECAP behaviours practiced in families: a pattern of mostly recommended behaviours, a pattern of behaviours aiming at the avoidance of allergens and a pattern of mixed, partially unhealthy behaviours. ECAP counselling should take these patterns into account.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on exposome

000941 | In vitro supporting diagnostic tools in plant-food allergy

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Background: Food allergy is a pathological state with the immune system reacting unusually to specific food allergens that can lead to severe, even life-threatening, reactions. From plant foods, Pru p 3, a non-specific lipid transfer protein (LTPs) of peach, is the primary sensitiser in LTP allergies in the Mediterranean population, causing severe reactions. Consequently, effective and early diagnosis is crucial. Several diagnostic methods are available, like circulating specific immunoglobulin E (sIgE) determination and skin prick test; however, the gold standard is oral food challenge. Other *in vitro* tools like basophil activation test (BAT) or mast cell activation test (MAT) have emerged to support diagnosis. Our objective is to establish and compare the value of sIgE, BAT, and MAT in LTP allergy diagnosis.

Method: Twenty-one patients sensitised to LTP and with peach allergy, and sixteen healthy controls were recruited. BAT was performed in whole blood with Pru p 3 at seven ten-fold concentrations. For MAT, Laboratory of Allergic Diseases 2 (LAD2) human mast cells were cultured with serum from allergic patients and controls, and stimulated with different concentrations of Pru p 3. Activation was evaluated through percentage of cells expressing CD63 (%CD63$^+$) by flow cytometry. Total IgE (tIgE) and sIgE were measured by ImmunoCAP.

Results: BAT and MAT showed significantly higher values of %CD63$^+$ in allergic patients than controls. In addition, both displayed great values of sensitivity (around 85%) and specificity (93%). Combination of BAT and MAT increased sensitivity up to 95% compared to the techniques individually. However, ImmunoCAP showed sensitivity values (cut-off >0.35 kUA/L) of 100% and 87.5% of specificity. Moreover, we observed that MAT is sIgE dose-dependent, showing a strong positive correlation (Spearman $r = 0.82$, $p < 0.0001$) while BAT showed a lower correlation (Spearman $r < 0.2$, $p > 0.05$).

Conclusion: BAT and MAT can be useful as *in vitro* complementary tools in the diagnosis of LTP-related allergy. In addition, together they both have a higher sensitivity than each one alone, and MAT has a strong correlation with sIgE levels. Despite of the difficulty of these cellular techniques, they show great diagnostic results in comparison to other non-functional techniques as immunoassay.

Conflicts of interest: The authors did not specify any links of interest.

000331 | Transcriptomics reveals a distinct metabolic profile in T cells from severe allergic patients

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Background: Mechanisms causing the onset and perpetuation of chronic inflammation in severe allergic patients remain unknown. Previous results suggested that severe allergic inflammation is linked to systemic alteration in sphingolipid, lysophosphocholine and glucose metabolism, together with an impairment of regulatory functions. Here, we aimed to identify transcriptomic alterations in T cells that could be associated with the degree of severity of allergic patients.

Method: T cells were isolated from severe ($n = 7$) and mild ($n = 9$) allergic patients, and control (non-allergic, healthy) subjects ($n = 7$) to perform RNA analysis by Affimetrix gene expression microarray. Significant transcripts were used to identify compromised biological pathways in the severe phenotype.

Results: The T cells' transcriptome of severe allergic patients was distinct from that of mild and non-allergic subjects. The severe allergic

group showed a greater number of differentially expressed genes (DEGs) vs control (4924 genes) and *vs* mild (4232 genes) groups. Mild allergics also had 1102 DEGs vs controls. Pathway analysis revealed alterations in metabolism and immune response in the severe allergic phenotype. Severe allergic patients presented downregulation in genes related to oxidative phosphorylation, fatty acid oxidation and glycolysis together with increased expression of genes coding inflammatory cytokines (e.g. *IL-19*, *IL-23A* and *IL-31*). Moreover, the downregulation of genes involved in TGFβ pathway together with a decreased number of T regulatory cells (CD4+CD25+), suggest a compromised regulatory function in severe allergic patients.

Conclusion: This study demonstrates a downregulation on metabolic and cell signalling pathways in T cells of severe allergic asthma patients associated with a diminished regulatory T cell function. These findings support a link between energy metabolism of T cells and allergic inflammation.

Conflicts of interest: The authors did not specify any links of interest.

000437 | Beta-lactoglobulin as allergy-protective lipocalin from farm dust: Searching its sources in bovine tissues

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Background: Growing up on a farm and consequent exposure to farm environment has been shown to prevent onset of asthma and allergies. Especially traditional dairy farm environment has been proven to be beneficial. Studying dust samples derived from cattle farms and ambient air, we detected significant amounts of the major whey protein beta-lactoglobulin (BLG). In context with ligand-sit acts tolerogenic and contributes to the allergy protective farm effect. In previous investigations we could reveal bovine urine as an unexpected source for this milk protein in the environment. This prompted us to investigate additional expression and production sites, outside the bovine udder.

Method: Tissue samples derived from both sexes (bovine udder, testis, kidney and adrenal gland) were tested for their BLG occurrence by immunohistochemical staining (IHC). Additionally, protein extracts of these organs were produced and tested by BLG-specific ELISA and immunoblot. Furthermore, RNA from tissues was extracted and tested with BLG-specific primer in reverse transcription PCR.

Results: BLG could be detected on the protein level in all tested tissues of both sexes with IHC, ELISA and immunoblot, in varying amounts. PCR results indicated that BLG besides in udder is expressed in testis, and to minor extents also in kidneys.

Conclusion: Our study shows that the udder is not the only production site of the milk protein BLG, but that this immune-modulatory protein was also expressed in tissues of male cattle. These results may explain why stables of both cattle sexes contribute to the allergy-protective farm effect.

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Conflicts of interest: EJJ is inventors on EP2894478, owned by Biomedical International R+D GmbH, of which she is shareholder.

000387 | Bioinformatics analysis of Fel d 1 reveals structural variability and target sequences for gene editing using CRISPR

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Background: Allergy to cat impacts a significant proportion of the population. Current treatments for cat allergy have limited or inconsistent effects. Here, we present an extensive bioinformatics analysis of the major cat allergen, Fel d 1. The aims are to assess the structural variability of Fel d 1 and to identify conserved sequences in the genes for the targeted deletion of Fel d 1 using CRISPR technology. The ultimate goal is to examine the evolution and potential function of the allergen, and to develop Fel d 1-free cats as a novel solution for cat allergy.

Method: Reference sequences for Fel d 1 chains 1 and 2 (encoded by genes *CH1* and *CH2*, respectively) were used to identify, assemble, and align the Fel d 1 sequences or homologs from 140 domestic and 136 exotic (non-domestic, e.g., tiger, lion, cougar) cat genomes. Pairwise identities with the Fel d 1 references, as well as amino acid (AA) substitutions and conserved sequence fragments were evaluated for each of the 38 cat species analyzed.

Results: Comprehensive analyses of >275 domestic or exotic cats identified >100 unique AA substitutions in Fel d 1 chains 1 and 2, with greater variability detected in chain 2 (24% and 57% of domestic and exotic cat chain 2 residues, respectively) versus chain 1 (17% domestic, 39% exotic). The substitutions were largely comprised of dissimilar AA changes (i.e., changes in residue charge or polarity), with approximately 75% and 55% of all chain 1 and chain 2 substitutions determined to be dissimilar, respectively. For all cat species analyzed, the dissimilar substitutions in chain 2 were found to be primarily concentrated at the dimer interface of the structure of recombinant Fel d 1. In domestic cats alone, multiple conserved regions of 40–80 nucleotides in length were identified in *CH1* and

CH2, and were deemed appropriate targets for gene editing using CRISPR-Cas9.

Conclusion: The results represent the most comprehensive bioinformatics analysis of any allergen gene(s) to date. Comparative analyses revealed that the Fel d 1 sequences and corresponding allergen structure vary considerably across the family *Felidae*, suggesting that the allergen is not conserved in evolution and thus potentially non-essential for cats. The possible absence of an essential biologic function coupled with the identification of CRISPR target regions in the genes indicate that Fel d 1 may be a suitable candidate for gene deletion, which could significantly benefit cat allergy sufferers.

Conflicts of interest: The authors did not specify any links of interest.

001656 | Bradykinin increases transendothelial water flow in vitro by modulating endothelial barrier function

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Background: Angioedema is defined as swelling of the skin or mucous membranes lasting several hours to days. A distinction is made between mast cell-mediated and bradykinin-mediated angioedema. The latter includes hereditary angioedema. Here, a genetic defect leads to an increased production of bradykinin. This in turn increases endothelial permeability and thus the flow of water from the intravascular space into the interstitium. However, the underlying mechanism here is not fully understood. This project therefore investigates the influence of bradykinin on cell-cell contacts (tight and adherens junctions) and the endothelial glycocalyx, important structures of the endothelial barrier.

Method: Human umbilical vein endothelial cells (HUVEC) were cultured on transwell filters and bradykinin was added. Subsequently, its influence on the endothelial barrier was analyzed. At the biophysical level, transendothelial electrical resistance (TEER) and apparent permeability factor were determined, transendothelial water flux was measured using the D2O dilution method. These were compared with changes in the expression and localization of components of the cell-cell contacts and glycocalyx. RT-PCR, Western blot, and immunocytochemistry were used for this purpose. The thickness of the glycocalyx was determined using the wheat germ agglutinin assay, and it was also enzymatically degraded to further investigate its influence on barrier function.

Results: Bradykinin significantly increased endothelial permeability, as indicated by a decrease in TEER and increase in apparent permeability factor. In addition, transendothelial water flux was significantly increased. Consistent with this, changes in the expression of cell-cell contact proteins, especially the tight junction protein claudin 5, were detected. Although bradykinin had no effect on the thickness of the glycocalyx, previous degradation of the glycocalyx led to a significantly increased effect of bradykinin on the endothelial barrier.

Conclusion: Bradykinin resulted in significant weakening of the endothelial barrier, which was accompanied by decreased expression of the tight junction protein claudin 5. In contrast, glycocalyx appears to be protective against bradykinin-mediated barrier damage. This may provide further approaches for the understanding of angioedema.

Conflicts of interest: J. Greve: has received speaker/consultancy fees from CSL Behring, Takeda and BioCryst. He has also received funding to attend conferences/educational events from CSL Behring and Takeda. He has participated as an investigator in a clinical trial/registry for CSL Behring, BioCryst and Takeda.J. Hahn: has received speaker/consultancy fees from CSL Behring and Takeda. She has also received funding to attend conferences/educational events from CSL Behring and Takeda. She has participated as an investigator in a clinical trial/registry for CSL Behring, BioCryst, Pharvaris and Takeda.R. Lochbaum: has received funding to attend conferences/educational events from CSL Behring, BioCryst and Takeda. He has participated as an investigator in a clinical trial for Takeda and Pharvaris.

000120 | Cross-reactivity studies between *Juniperus oxycedrus* and *Cupressus arizonica* pollen extracts reveal the presence of species-specific allergenic components in *J. oxycedrus*

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Background: Allergy to Cupressaceae pollen is common worldwide. The main species include *Cupressus arizonica* and *C. sempervirens*, *Juniperus ashei* and *J. oxycedrus*, which is highly prevalent in Spain and the Mediterranean basin. Group 1 allergens (pectate lyase) are considered the most important cross-reactive allergens in the Cupressaceae pollen family and responsible for co-sensitization to several Cupressaceae species. The role of allergens different to group 1 in the allergy to Cupressaceae pollen, have not been studied before. The objective of this study was to explore the molecular basis of cross-reactivity between *J. oxycedrus* and *C. arizonica* pollen extracts.

Method: Sera from Spanish allergic patients ($n = 12$) sensitized to Cypress pollen, residing in Burgos, Spain were obtained. Allergenic extracts from *J. oxycedrus* and *C. arizonica* pollen were prepared by extraction in PBS. Pectate lyase in the extracts was precipitated with ammonium sulfate and purified by affinity and anionic exchange chromatography. Sensitization to *J. oxycedrus*, *C. arizonica*, Jun o 1 and Cup a 1, was tested by ELISA and Westernblots. Cross reactivity was evaluated by ELISA Competition. IgE reactive components in the extracts were detected by Westernblot and inhibition experiments with individual sera. The proteome of the extracts and relative abundance of each protein was analysed by mass spectrometry.

Results: A significant correlation was observed between serum specific IgE titres for *J. oxycedrus* versus *C. arizonica* ($r = 0.9495$; $p < 0.001$) and Jun o 1 *versus* Cup a 1 ($r = 0.9748$; $p < 0.001$). ELISA competition with a serum pool showed that *J. oxycedrus* extract inhibited 93% of the IgE reactivity to *C. arizonica*. Additionally, *C. arizonica* inhibited 74% of the IgE reactivity to *J. oxycedrus*. Jun o 1 and Cup a 1 were the most abundant quantitatively. Several homologue proteins are present in both extracts, including official and putative allergens. Westernblot and inhibition experiments with individual sera revealed several IgE reactive bands in *J. oxycedrus* and *C. arizonica*. IgE response against *J. oxycedrus* involves Jun o 1 and other molecules such as a 38 to 40 kDa band and a 29 kDa band.

Conclusion: IgE sensitization to *J. oxycedrus* and *C. arizonica* occurs against several proteins, including group 1 allergens. In the group of 12 patients analysed in this study, the allergic response is directed against cross-reactive and *J. oxycedrus*-specific allergens. Pharmaceutical preparations for diagnosis and immunotherapy should include the relevant allergens.

Conflicts of interest: The authors did not specify any links of interest.

001376 | Differential signaling in human immune cells induced by immunomodulatory commensal archaea

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Background: Early childhood exposure to a diverse microbial environment is inversely related to the development of asthma and allergies, strongly implying a causal role for microbiota typically associated with farm-like environments.[1,2] Presence of different archaeal strains (*e.g.*, *M. stadtmanae* and *M. smithii*), among others, within this microbiome or in stool samples of children has been associated with reduced odds ratio of allergic diseases.[3,4] However, although both archaeal strains activate cells via their RNA and are recognized through TLR8, they possess a strikingly different capacity to induce inflammatory cytokine secretion from human immune cells.[5,6] In order to get a more complete picture of their capacity to activate human immune cells, we performed an in-depth analysis of mRNA induction by both *M. stadtmanae* and *M. smithii* in PBMCs from healthy donors. The objective of this study is to identify and differentiate innate immune activation upon recognition of *M. stadtmanae and M. smithii*.

Method: Peripheral blood mononuclear cells (PBMCs) from healthy donors were stimulated with either *M. stadtmanae* and *M. smithii* and profiled by RNAseq analysis and multiplex ELISA.

Results: As already shown by us with other cells, stimulation with *M. stadtmanae* displays much higher activity, drives Th1 polarization in naïve T-cells and elicits a strong Th1 and IL-10 effector response from PBMCs. However, a set of specific cytokines such as IFN-beta, MCP-1 or IP-10 are induced by *M. smithii* in comparable strength. Furthermore, a small set of genes is induced by *M. smithii* only.

Conclusion: Taken together, our results indicate that the immune response-inducing capacity of archaea is not dictated by their TLR8-dependent RNA recognition alone.

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000316 | Intracellular expression of chemokine receptors CCR5, CCR6 and CCR10 in human basophils

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Background: Basophils are circulating granulocytes with known involvement in type 2 inflammation observed in tissues; however, their migration potential remains to be resolved. Resting basophils are known to express the chemokine receptors: CC chemokine receptors CCR1, CCR2, CCR3, CRTh2 and C-X-C chemokine receptor type 1 (CXCR1), CXCR2 and CXCR4. Recently, we also found that anti-IgE activated and degranulated basophils express CCR4, CCR8, CCR9, atypical chemokine receptor 4 CCX-CKR and XC chemokine receptor XCR1. Therefore, we aimed at investigating chemokine receptors' surface and intracellular expression on resting and anti-IgE-activated basophils.

Method: Whole blood of non-allergic individuals ($n = 3–5$) was stimulated with non and 1000 ng/mL anti-IgE for 30 min. Surface and intracellular expression of a selected panel of chemokine receptors, identification- and activation markers were evaluated using flow cytometry.

Results: We confirmed intermediate surface expression of CD203c and CXCR4 on resting basophils and intracellular expression of CD63, a marker of secretory granules. Surprisingly, compared with FMO controls, unstimulated basophils showed intracellular expression (>40-100%) of the chemokine receptors CCR4, CCR5, CCR6, CCR8, CCR9, CCR10, CXCR4, CCX-CKR, and XCR1. In addition, we confirmed the anti-IgE-induced surface expression of CCR4 (41%), CCR8 (29%) and XCR1 (14%) on degranulated ($CD63^+$) basophils, as well as CCX-CKR (37%) and CXCR4 (33%). Notably, CCR5 and

CCR6 were not found on the surface of resting or degranulated basophils following anti-IgE activation. However, following anti-IgE stimulation, intracellular CCR6 expression was reduced compared to unstimulated basophils (MFI values: 528 and 1031, respectively), suggesting the release or degradation of CCR6. Interestingly, an unaltered intracellular expression of CCR4, CCR8, and CXCR4 was found after anti-IgE activation of basophils.

Conclusion: Intracellularly detected chemokine receptors in resting basophils suggest that CCR5, CCR6 and CCR10, together with CCR4, CCR8, CCR9 and XCR1, are pre-formed, highlighting that the human basophil has the potential to bind a broad spectrum of chemokines.

Conflicts of interest: The authors did not specify any links of interest.

000268 | Iron-binding features of birch pollen allergen Bet v 1 reduce its allergenicity and foster an anti-inflammatory tolerogenic phenotype in human monocytes

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Background: Bet v 1 is the major allergen in birch pollen to which up to 95% of patients sensitized to birch respond. As a member of the Pathogenesis-related PR 10 protein family, its natural function is implicated in plant defense, with iron-deficiency linked to its upregulation. In this study we assessed the capacity of Bet v 1 to sequester iron and its subsequent immunomodulatory properties by nourishing human immune cells

Method: Binding of Bet v 1 to iron quercetin complexes FeQ2 was analyzed in docking calculations and by spectroscopy. Serum IgE-binding to Bet v 1 with (holoBet v1) and without ligands (apoBet v 1) was assessed by ELISA, blocking experiments and Western Blot. Crosslinking-capacity of apo/holoBet v 1 was assessed on human mast cells, and their capacity to activate Arylhydrocarbon receptor (AhR) using the human reporter cell line AZ-AHR. Human PBMCs were stimulated with apo- and holoBet v 1 and assessed for labile iron and phenotypic changes by flow cytometry.

Results: Bet v 1 strongly bound to FeQ2 with calculated Kd values of 1 nm, surpassing affinities to quercetin alone nearly by a factor of 1000. Binding to FeQ2 masked IgE epitopes, thereby decreasing IgE binding up to 80% and impairing degranulation of sensitized human mast cells. Bet v 1 shuttled FeQ2 complexes into human monocytic cells, of which quercetin activated the anti-inflammatory AhR pathway, while Fe(III) increased the labile iron pool associated with an anti-inflammatory phenotype in CD14+monocytes and downregulation of HLADR.

Conclusion: To summarize, we reveal for the first time that FeQ2 binding reduces the allergenicity of Bet v 1 due to epitope masking, but also actively contributes anti-inflammatory stimuli to human monocytes, thereby fostering tolerance. Nourishing immune cells with complex iron may thus represent a promising antigen-independent immunotherapeutic approach to improve efficacy in allergen immunotherapy.

Conflicts of interest: F.R.-W., L.F.P. and E.J.-J. declare inventorship of EP2894478 (Roth-Walter F et al., Method and means for diagnosing and treating allergy.) (applicant Biomedical International R+D GmbH, Vienna, Austria). E.J.-J. declares shareholdership in Biomedical Int. R+D GmbH, Vienna, Austria. F.R.-W. received research funding from Biomedical International R+D GmbH, Vienna, Austria, Bencard Allergie GmbH, Munich, Germany and Vienna, Austria, and Allergy Therapeutics, Worthing, UK. Moreover, she received lecture honoraria by Bencard Allergie GmbH, Munich, Germany and Vienna, Austria, and Allergy Therapeutics, Worthing, UK. The other authors declare no relevant conflict of interest in relation to this abstract

000167 | Prophylactic vaccination against peanut allergy

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Background: Primary prevention of allergy by prophylactic immunotherapy might be seen as the ultimate goal of drug development in our area. None of the attempts undertaken so far revealed convincing results. Integrating allergens within virus-like particles (VLPs) harnesses the properties of a viral structure to stimulate a long-lasting, humoral immune response introducing the concept of prophylactic vaccination into allergy. We have previously demonstrated the immunogenicity and the cross-protective capacity of a VLP-Ara h2 (VLP Peanut) based-immunization in a murine model for peanut allergy. VLPs are well-established vaccine platforms inducing prompt, long-lasting, and powerful humoral and cellular immune responses. To test the hypotheses of prophylactic vaccination against peanut allergy, the vaccine was applied in a prophylactic immunization setting in mice.

Method: VLP-Peanut uses cucumber mosaic virus-like particles ($CuMV_{TT}$-VLPs), incorporating an engineered universal T cell epitope

derived from a tetanus toxin (TT), genetically fused with Ara h 2 ($CuMV_{TT}$-Arah2), co-expressed and purified in *E. coli*. Naïve BALB/c mice were first immunized with VLP Peanut via s.c. route. Two weeks after the last vaccine dose, mice were sensitized to peanut. Systemic challenge experiments were performed with peanut extract injected via i.v. route. The serum levels of anti-Ara h 2 IgG and IgE in mice were measured by ELISA.

Results: Mice vaccinated with VLP Peanut were protected against anaphylaxis upon systemic challenge with whole peanut. Anti-Ara h 2 IgG in mice immunized with VLP Peanut were significantly higher than control mice 14 days after sensitization, prior to challenge. Furthermore, no significant changes were detected in anti-Ara h 2 IgE levels measured two weeks after systemic challenge.

Conclusion: Once immunized with VLP Peanut, natural allergen exposure may maintain protective levels of IgG antibodies against peanut allergy. The results clearly indicate the ability to de-risk systemic anaphylaxis through prophylactic administration of VLP Peanut. This exciting finding opens a gateway of primary prophylaxis of allergy by VLP-based allergy vaccination.

Conflicts of interest: The authors did not specify any links of interest.

100026 | Automatic pollen monitoring in Europe

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Background: Automatic pollen monitors are being deployed and implemented in Europe. The instruments have developed from EU-defined technical readiness level 3 "proof of principle" to level 7 "system prototypes demonstrated in an operational environment" and beyond. Indeed, 3 automated pollen monitoring networks are operational in Europe (Germany, Switzerland, and Serbia), and more are yet to come. Of course, not all systems are perfect, but the current level achieved by the instruments mostly outperforms the common manual human system.

Method: What is important?

Results:

1. Which location? The location of setting up a pollen and spore monitoring station is as important as the question which instrument, manual or automatic. Recommendations for selecting good monitoring sites were developed.
2. Which instrument? The recent EU-wide EUMETNET Autopollen project evaluated the performance of all currently known automatic pollen monitors in the world.
3. Which algorithm? Can you use a single algorithm that covers all (or most) species? There are systems with many algorithms, one of which seems to be good for certain pollen species but perform poorly for other.
4. Although some well-trained humans are currently still better than some instruments at pollen recognition, the needed time for analysis or proper training is often lacking, data reporting is slow, but most importantly, the instrument that is used for manual pollen and spore sampling has some serious errors. In all, an error (excluding human error) of about 40% of the manual system is common.

Conclusion: Thus, automatic pollen monitoring has some advantages, which are now being acknowledged and it is only a matter of time when the new systems become established.

What are the next step developments to be expected in automatic pollen monitoring? Firstly, the establishment of high-performing (high price) monitors in networks across Europe. Secondly, a European wide network (infrastructure) of exchange for automatic online and at no cost pollen data, and thirdly, a new way of treating allergy patients. The basis for this improvement in patient care and, of course, doctors care (by alleviating allergist's normal daily load of work by eliminating the many "simple" allergic individuals), are the algorithms used to assist local general practitioners to treat their allergic patients themselves. This frees up time of allergologists to focus on the difficult cases, of which are already many.

These new developments will be discussed and data supporting the findings will be presented. Welcome to a new world of serving both, the allergic individuals and the specialists who treat them!

Conflicts of interest: The authors did not specify any links of interest.

100508 | Impact of environmental air pollution on the fractional exhaled nitric oxide measurements in children

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Background: Air pollution is a significant environmental health concern, especially for children who are more susceptible to its adverse effects. Fractional exhaled nitric oxide (FeNO) measurements have emerged as a non-invasive biomarker for evaluating airway inflammation (primary of eosinophilic orgin) and could potentially be used to monitor the impact of air pollution on respiratory health.

The impact of air pollution on FeNO measurements in children is not well understood. We know a lot about patient-related factors such as genetics, sex, weight, height, diet, medication (including anti-inflammatory drugs), tobacco smoke exposure, and atopy but limited knowledge exists regarding environmental factors that may influence these test results. To address this gap, this study aimed to investigate the impact of exposure to primary NOx (mixtures of NO_2 and NO) and other pollutants on FeNO test values.

Method: The study involved 84 children between the ages of 10 and 15 (mean age 12.57 years), divided into three groups. All the groups were similar in terms of age, sex, weight, and height. Of these

children, 22 were from Cieszków, a non-polluted village in Lower Silesia, while the remaining 62 were from Katowice, a more polluted city of about 300,000 in Upper Silesia. FeNO measurements were taken during the summer for the Cieszków group and a group of 26 children from Katowice, and during the autumn for a group of 36 children from Katowice. Additionally, all subjects completed a questionnaire to provide information about their exposure to pollutants. The study utilized air pollution data obtained from the closest monitoring stations of the Polish Chief Inspectorate of Environmental Protection.

Results: We found that the mean FeNO value for children in Cieszków was 4.5 ppm with a measured NOx of 4. For the spring group from Katowice, the mean FeNO value was 11.7 ppm with a measured NOx of 25, and for the autumn group, the mean FeNO value was 29.8 ppm with a measured NOx of 70.

Conclusion: In our study, we observed a strong correlation between NOx levels in the environment and FeNO measurements, which is not evident in other studies. We propose that FeNO measurements may have some limitations, as environmental pollution can significantly influence them, particularly when FeNO is measured soon after entering a building.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on rhinits and rhinosinusitis

000998 | Characteristics of patients with chronic rhinosinusitis with nasal polyps who did or did not undergo functional endoscopic sinus surgery: A US real-world retrospective cohort study

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Background: There are limited data regarding the characteristics of patients with chronic rhinosinusitis with nasal polyps (CRSwNP) who undergo functional endoscopic sinus surgery (FESS) compared to those who do not. The aim of this study was to report the baseline characteristics of CRSwNP patients who underwent FESS vs no-FESS in real-world settings in the US.

Method: Retrospective cohort study of patients with CRSwNP undergoing or not undergoing FESS in US real-world practice (Optum claims data 2011–2021). Patients with biologic therapy, FESS/polypectomy, or nasal cavity/sinus cancer in the previous 12 months were excluded. Demographics were assessed on index date, and comorbidities/medication use over the 12 months pre-index.

Results: This analysis comprised 9,305 FESS patients and 34,446 risk-set-matched non-FESS patients. Overall, 57% of patients were male and 75% were White. FESS patients were younger than non-FESS patients (mean [SD] age 52 [17] vs 57 [17] years, $p < 0.01$) with a lower proportion ≥65 years of age (29% vs 39%, $p < 0.01$), and more likely to be commercially insured (69% vs 59%, $p < 0.01$). In both the FESS and non-FESS groups, a high proportion of patients had a diagnosis of acute sinusitis (47.2% [FESS group] vs 33.5% [non-FESS group], $p < 0.01$), allergic rhinitis (51.9% vs 53.1%, $p = 0.05$), asthma (25.7% vs 29.8%, $p < 0.01$), sleep disorders (21.1% vs 20.0%, $p = 0.02$), depression (12.9% vs 12.1%, $p = 0.03$), and anxiety (13.9% vs 13.8%, $p = 0.86$). A high proportion of patients used oral corticosteroids (OCS) (64.6% [FESS] vs 52.2% [non-FESS] [$p < 0.01$]) and antibiotics (44.9% [FESS] vs 39.4% [non-FESS] group [$p < 0.01$]). Leukotriene antagonists prescriptions were filled or administered in 20.9% of FESS vs 24.6% of non-FESS patients ($p < 0.01$), antihistamines in 21.4% of FESS vs 20.4% of non-FESS patients ($p = 0.03$), and non-steroidal anti-inflammatory drugs in 24.5% of FESS vs 23.3% of non-FESS patients ($p = 0.02$).

Conclusion: In US clinical practice, although CRSwNP patients undergoing FESS appear to have more acute sinusitis and greater use of OCS and antibiotics, both patients who do and do not undergo FESS have significant comorbidity and systemic treatment burden.

Conflicts of interest: SEL: AstraZeneca, Genentech, GlaxoSmithKline, Novartis, Regeneron Pharmaceuticals, Inc., and Sanofi – advisory board member; Allakos, AstraZeneca, GlaxoSmithKline, Knopp Biosciences, Sanofi – clinical trial funding ATP: AstraZeneca, Regeneron Pharmaceuticals, Inc., and Sanofi – advisory board member; Optinose, Regeneron Pharmaceuticals, Inc., and Sanofi – research grants; GlaxoSmithKline and Optinose – consultant PHH: Regeneron Pharmaceuticals, Inc. and GlaxoSmithKline – speaker fees; GlaxoSmithKline – clinical trial funding; Slate Therapeutics and Stryker – consultant; SoundHealth – equity interest SR: GlaxoSmithKline, Novartis, and Sanofi – consultant, research grant, and honoraria; EPOS and European Chronic Rhinosinusitis Outcome Registry – steering committee member AHK, DLI, NP-I, and JAJ-N: Sanofi – employees/may hold stock and/or stock options SN: Regeneron Pharmaceuticals, Inc. – employees/may hold stock and/or stock options

001037 | Impact of functional endoscopic sinonasal surgery on oral corticosteroid burden and healthcare resource utilization in patients with chronic rhinosinusitis with nasal polyps in US real-world practice

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Background: The impact of functional endoscopic sinonasal surgery (FESS) on oral corticosteroid (OCS) burden and healthcare resource utilization (HCRU) for patients with chronic rhinosinusitis with nasal polyps (CRSwNP) is understudied. In this study, we investigated the differences in OCS burden and HCRU between patients with CRSwNP who underwent FESS compared with those who did not in real-world settings in the US.
Method: Retrospective cohort study of CRSwNP patients using US claims data (Optum; 2011–2021). FESS and non-FESS groups were propensity score matched to adjust for confounding. The intervention period was Day 0–44 and the follow-up period was Day 45–365 post-index. OCS burden (cumulative dose in mg prednisone equivalents), other medications, HCRU, and costs were compared among FESS vs non-FESS patients in the 1-year post-surgery period.
Results: Each group included 8,909 patients. During follow-up, OCS use was marginally lower among FESS vs non-FESS patients (mean difference in cumulative dose: −40 mg [95% CI −64, −16] per patient); however, OCS burden remained high in each group among patients who filled an OCS prescription (34.6% vs 36.0%), with mean (SD) cumulative dose of 521 (786) mg vs 612 (906) mg, respectively. Mean total healthcare costs were $28,832 (FESS group) and $2,537 (non-FESS group) during the intervention period but similar during follow-up ($15,659 and $15,926). HCRU was similar in the follow-up period, except that more FESS than non-FESS patients visited an otolaryngologist (57.5% vs 32.0%). During follow-up, FESS patients had a significantly increased likelihood of having a polypectomy procedure (odds ratio [95% CI] 5.74 [4.89, 6.74]) or an endoscopy (3.63 [3.40, 3.88]); 10.9% of FESS and 2.1% of non-FESS patients had a polypectomy, and 47.6% of FESS and 20.0% of non-FESS had an endoscopy. Overall, 20.7%, 22.5% and 29.2% of all patients filled a prescription for leukotriene antagonists, non-steroidal anti-inflammatory drugs, and oral antibiotics, respectively.
Conclusion: Although FESS led to a lower OCS use among patients with CRSwNP, OCS burden remained high in both FESS and non-FESS patients, with similar costs in the follow-up period.

Conflicts of interest: SEL: AstraZeneca, Genentech, GlaxoSmithKline, Novartis, Regeneron Pharmaceuticals, Inc., and Sanofi – advisory board member; Allakos, AstraZeneca, GlaxoSmithKline, Knopp Biosciences, Sanofi – clinical trial funding ATP: AstraZeneca, Regeneron Pharmaceuticals, Inc., and Sanofi – advisory board member; Optinose, Regeneron Pharmaceuticals, Inc., and Sanofi – research grants; GlaxoSmithKline and Optinose – consultant PHH: GlaxoSmithKline and Regeneron Pharmaceuticals, Inc. – speaker fees; GlaxoSmithKline – clinical trial funding; Slate Therapeutics and Stryker – consultant; SoundHealth – equity interest SR: GlaxoSmithKline, Novartis, and Sanofi – consultant, research grant, and honoraria; EPOS and European Chronic Rhinosinusitis Outcome Registry – steering committee member DLI, AHK, NP-I, and JAJ-N: Sanofi – employees/may hold stock and/or stock options SN: Regeneron Pharmaceuticals, Inc. – employees/may hold stock and/or stock options

001343 | Mouse model of neutrophilic non-type 2 CRS: The superior effect of *Staphylococcus aureus* compared with *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*

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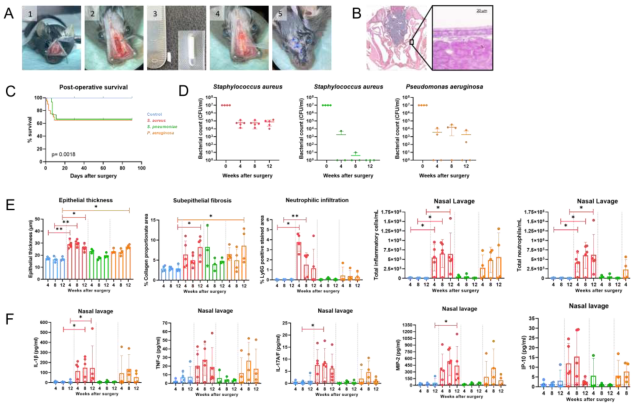
Background: Chronic rhinosinusitis (CRS) is an inflammatory respiratory disease with symptoms of nasal blockade, headache, loss of smell and nasal secretions that last for at least 12 weeks. It affects 11% of European population and is a global health burden. CRS is classified according to its inflammatory profile as Type 2 eosinophilic or non-Type 2 neutrophilic CRS. Currently, the pathogenesis of CRS is not fully understood, especially regarding non-Type 2 CRS, and no validated mouse models are available to study its disease mechanisms. In order to explore pathophysiological mechanisms of non-Type 2 CRS, we aimed at establishing a neutrophilic mouse model of bacterial-induced CRS.
Method: A nasal tampon was micro-surgically inserted in the nasal cavity of 72 mice and was then inoculated with 10 µL of 10^8 CFU/mL solution of three different bacteria relevant to sinus disease: *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*. Inflammatory features in the nasal mucosa were evaluated after 4, 8 and 12 weeks on decalcified skulls by means of histology. Antibodies were measured in nasal lavage and bronchoalveolar-lavage by ELISA. Differential cell-counts and cytokines measurements were performed in the NL. Kruskal-Wallis test was applied for statistics.
Results: Post-operative mortality was more important for *S. pneumoniae* than for *P. aeruginosa*. While *S. aureus* and *P. aeruginosa* were still detectable in the nasal lavage after 4, 8 and 12 weeks post-surgery,

S. pneumoniae seemed to be cleared. Mice with *S. aureus*-induced experimental CRS showed a significant increase in the epithelial thickness (4w: $p = 0.0012$; 8w: $p = 0.0045$; 12w: $p = 0.0204$), subepithelial fibrosis (12w: $p = 0.0131$), and neutrophilic infiltration (4w: $p = 0.01444$; 8w: $p = 0.0042$) at the level of the nasal mucosa, with increased IL-1β (8w: $p = 0.0262$; 12w: $p = 0.0384$), TNFα (ns), IL-17 (8w: $p = 0.0113$), MIP-2 (12w: $p = 0.0438$) and IP-10 (ns). Mice with *P. aeruginosa*-induced experimental CRS showed significantly increased epithelial thickness (12w: $p = 0.0125$) and subepithelial fibrosis (12w: $p = 0.0225$). Mice with *S. pneumoniae*-induced experimental CRS did not show any inflammatory changes.

Conclusion: *S. aureus* is the most potent inducer of neutrophilic non-Type 2 CRS in a mouse model of bacterial-induced CRS. This mouse model allows us to further investigate the pathogenesis of non-Type 2 CRS.



A. Surgical technique for the induction of neutrophilic inflammation at the level of the maxillary sinuses in the nasal mucosa of mice. B. Pilot experiment confirming the presence of the nasal tampon does not induce any inflammation in the maxillary sinuses epithelial layer. C. Survival curve for mice treated with saline (control), *Staphylococcus aureus, Streptococcus pneumoniae and Pseudomonas aeruginosa*. D. Presence of the different bacteria in the nasal lavage of mice after 4, 8 and 12 weeks post-surgery. E. Inflammatory features of mice with experimental neutrophilic CRS after 4, 8 and 12 weeks post-surgery. F. Cytokine induction in the nasal lavage of mice with experimental neutrophilic CRS.

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Conflicts of interest: The authors did not specify any links of interest.

000179 | The correlation between visual analogue scales, total nasal symptom scores and peak nasal inspiratory flow in children and adolescents with perennial allergic rhinitis

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Background: Allergic rhinitis (AR) is a common allergic disease in children. Symptoms monitoring is important to adjust treatment. In adults VAS is well validated for measurement of AR symptoms which correlated well with total nasal symptom score (TNSS) and significantly negative correlated with peak inspiratory flow (PNIF). However, the study in children was limited. Our study aimed to assess the correlation between VAS, TNSS and the objective outcome, PNIF measurement, in children and adolescents with perennial allergic rhinitis (PAR) and to compare VAS and TNSS of children with parent assessed VAS (P-VAS).

Method: Patients with PAR, aged 6–18 years, were followed for 8 weeks. Patients and their parents recorded a daily electronic diary, including the evaluation of VAS, TNSS and patientsalso recorded the PNIF measurement daily. The correlations between VAS from patient, P-VAS, TNSS, and Z score of PNIF (adjusted for age and sex) were analyzed using Spearman's rank correlation coefficient (r_s). The significant level was $p < 0.05$. The agreement of VAS and TNSS between severity group was obtained by the *Cohen's Kappa*.

Results: A total of 2046 electronic diary records from 38 patients (52% male) aged 6–18 years with PAR were obtained. A moderate correlation between VAS and TNSS ($r_s = 0.493$; $p < 0.001$) and between P-VAS and TNSS ($r_s = 0.419$; $p < 0.001$) were found. There was a very weak negative correlation between VAS, TNSS, P-VAS and PNIF ($r_s = -0.159$, $r_s = -0.164$, $r_s = -0.146$; $p < 0.001$ respectively). The weak negative correlation between nasal congestion symptom and PNIF was found ($r_s = -0.211$; $p < 0.001$) as shown in Table 1. However, our study showed a strong correlation between VAS and P-VAS ($r_s = 0.815$; $p < 0.001$). The correlation between VAS, P-VAS, and TNSS is stronger in children than in adolescents. The moderate to severe PAR had a stronger correlation between VAS, P-VAS and TNSS than the mild PAR. Fair agreement of VAS and TNSS was found between mild and moderate to severe severity group (Kappa = 0.293; $p < 0.001$).

Conclusion: In children and adolescents with PAR, symptom monitoring based on subjective measurements may be insufficient. We propose symptom monitoring with subjective measurements such as VAS, TNSS together with an objective measurement, which is PNIF, to improve the quality of the treatment.

Table I The correlations between VAS, parent-assessed VAS, TNSS and PNIF

			Spearman's rank correlation coefficient	p Value**
VAS	vs	P-VAS	0.815	< 0.001
VAS	vs	TNSS	0.493	< 0.001
VAS	vs	PNIF*	-0.159	< 0.001
TNSS	vs	P-VAS	0.419	< 0.001
TNSS	vs	PNIF*	-0.164	< 0.001
P-VAS	vs	PNIF*	-0.146	< 0.001

P-VAS = parent-assessed VAS
*PNIF was Z score of PNIF (adjusted for age and sex)
**Correlation is significant at the 0.05 level (2-tailed).

Conflicts of interest: The authors did not specify any links of interest.

001109 | The effect of novel inflammation markers in patients with nasal polyps

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Background: The etiology of nasal polyp (NP) is unclear. Some theories have suggested that polyps arise as a result of conditions that cause chronic inflammation of the nose and nasal sinuses, characterized by stromal edema and variable cellular infiltrate. Many authors have attempted to identify independent risk factors for recurrence of NPs. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have been identified as potential markers for determining inflammation. In this study, we aimed to investigate how inflammation markers such as lymphocyte-monocyte ratio (LMR), eosinophil-lymphocyte ratio (ELR) as well as NLR and PLR are affected in rhinitis patients.
Method: This retrospective case-control study included 141 patients with nasal polyps 162 patients without nasal polyps matched for sex and age. We examined the patient files in terms of radiological and laboratory data. Patients were classified by paranasal sinus CT scans and divided into two groups according to their radiological findings: chronic sinusitis patients with NP (CRSwNP) and chronic sinusitis patients without NP (CRSwoNP). NLR, PLR and differential blood counts and demographic characteristics of the patients were analyzed. Serum inflammation markers and all variables were compared between the two groups.
Results: Age (35.6 ± 10.6, 32.9 ± 10.3, $p = 0.445$), gender (63 %44.7, 89 %54.9 female, $p = 0.075$) and body mass index (31.2 ± 3.2, 31 ± 3.08) in all groups, $p = 0.229$) respectively (with and without polyps, p-value). Asthma was diagnosed in (37 26.2%, 17 10.5%, $p < 0.001$) and Lund-Mackay score (8.9 ± 0.5, 2.8 ± 0.4, $p < 0.001$) were higher in CRSwNP compared to CRSwoNP. Lymphocyte count (2.82 ± 0.8, 2.35 ± 0.6, $p < 0.001$), platelet count (302.4 ± 76.1, 268.6 ± 49.8, $p < 0.001$), eosinophil count (302.4 ± 76.1, 268.6 ± 49.8, $p < 0.001$) were significantly higher in CRSwNP. PLR (116.7 ± 44, 121.3 ± 35.8, $p = 0.001$), LMR (6.48 ± 2.5, 5.37 ± 1.9, $p = 0.006$), ELR (0.124 ± 0.1, 0.111 ± 0.8, $p = 0.002$), were significantly different respectively (with polyps, without polyps).
Conclusion: Nasal polyps develop as a result of chronic inflammation in the nasal passage. Despite growing evidence that bacteria, fungi, allergens and superantigens play important roles in the pathophysiology of CRSwNP, the exact cause of polyposis still remains unknown. Moreover, the etiology of NPs is considered multifactorial. Increased systemic inflammation provides important prognostic information for many diseases. In our study, we found that lymphocyte, thrombocyte, eosinophil, LMR and ELR values were significantly increased in patients with polyps compared to the group without polyps.
Conflicts of interest: The authors did not specify any links of interest.

001610 | Experience with dupilumab in the treatment of CRSwNP in a Hungarian center

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Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a predominantly type 2-mediated inflammatory disease with reduced health-related quality of life (HRQoL). Dupilumab, a fully human monoclonal antibody that binds IL-4Rα and inhibits signaling of both IL-4 and IL-13, has shown efficacy across multiple diseases with underlying type 2 signatures: asthma, atopic dermatitis, and chronic sinusitis with nasal polyposis. In Hungary based on the EPOS 2022 and EUFOREA, the criteria of indication were elaborated. Patient are selected in the CRS centers according to these criteria, and the treatment starts when the named patient reimbursement is accepted by the National Health Insurance Company. We report our provisional findings from a real-life, prospective observational cohort about the therapeutic efficacy of dupilumab in an adult CRSwNP-population (≥18 years) in our center.
Method: Since 2020 all together 45 patient got named patient reimbursement of dupilumab and were treated at the ENT Department of the University of Szeged. Dupilumab was auto-administered subcutaneously, 300 mg once in every 2 week. We registered 22- item Sinonasal Outcome Test (SNOT22), rhinosinusitis severity visual analoge scale (VAS), NOSE questionarre, we performed nasal endoscopy and evaluated nasal polyp score and smell disorderat baseline, 6 months (t1) and 12 months (t2) follow up.
Results: 26 male 19 female patient are treated with dupilumab continously, avarage age 53.75 years. At baseline, patients had poor quality of life: the mean nasal polyp score was 4,77, SNOT22 (0–110) 66,53, VAS (0–10) 8,378. The number of previous surgeries (FESS) was 4,53. 33 patients have asthma, 29 have comorbid non-steroidal antiinflammatory drug-exacerbated respiratory disease (NSAID-ERD). After 3 months all of them experienced improvement in nasal airflow, and less postnasal drip. At 6 months follow up visit all the examined parameters improved significantly. SinoNasal Outcome

Test-22 (SNOT-22) improved from 66,53 to 16,45, bilateral Nasal Polyp Score (NPS) improved from 4,77 to 1,22. At 12 months follow up visit all these improvements were maintained. No rescue treatment or surgery was necessary. Only one patient had hypereosinophilia, but with the administration of dupilumab in every third week it normalised.

Conclusion: Dupilumab treatment led to significant improvement in symptoms and the quality of life in this difficult-to-treat group of patients, without any severe side effect. It is a promising therapeutic option for uncontrolled CRSwNP patients.

Conflicts of interest: The authors did not specify any links of interest.

001295 | Response to treatment with dupilumab in patients with asthma and/or chronic rhinosinusitis and nasal polyposis (CRScNP)

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Background: Dupilumab is a fully human monoclonal antibody aimed at IL-4 receptor-α, inhibiting both IL-4 and IL-13 signaling.

Dupilumab is indicated in adults and adolescents 12 years of age and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterized by elevated blood eosinophils and/or elevated fractional exhaled nitric oxide (FeNO) which are not adequately controlled with high-dose inhaled corticosteroids (ICS) in combination with another medication for maintenance treatment.

In addition, dupilumab is indicated as add-on to intranasal corticosteroids for the treatment of adults with severe CRScNP for whom systemic corticosteroid therapy and/or surgery do not provide adequate disease control.

Method: We present the results of an observational and prospective study in which we included 29 patients diagnosed with asthma with or without CRScNP treated with dupilumab and reassessed at least 16 weeks after the start of treatment.

Our aim was to assess the response to dupilumab measuring the following variables: age, sex, pre-bronchodilator FEV1, FeNO, asthma control test (ACT), blood eosinophils, presence of polyps on anterior rhinoscopy (AR), SNOT22 score, prior number of polipectomys, prior treatment with another biologic agent.

Results: Our population mean age was 47.6 years and 16 were women (52%). Mean baseline blood eosinophils was 491.6, total IgE 698.5 and FeNO 46.3. Sixteen patients had nasal polyposis. Of these patients, nine had undergone an operation on at least one occasion. Fourteen had prior treatment with another biologic agent: 11 mepolizumab and 2 omalizumab.

We compare the parameters collected at baseline, 16 weeks from the start of dupilumab.

Blood eosinophils count increased in three patients but had no related symptoms. A significant and rapid improvement in asthma control was obtained. The median ACT score increased from 16 to 21. The median FEV1 increased from 79% to 85%.

Regarding patients with polyposis, SNOT22 decreased from 49 to 5 and the number and volume of polips improve in 100% of patients.

Conclusion: The response to treatment with dupilumab was excellent and rapid, achieving improvements in the aforementioned variables from the first sixteen weeks after initiation.

However, we will continue to monitor these patients and add new patients to this study and thus be able to draw better conclusions about this treatment.

Conflicts of interest: The authors did not specify any links of interest.

100076 | Extrarespiratory symptoms in patients with severe pollen allergy: An underrecognized problem uncovered by a year-long diary survey in Japan

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*Presenting author: Y. Fukutomi

Background: Although the most common symptoms of pollen allergy are rhinitis and conjunctivitis, in clinical practice we sometimes encounter severe pollen allergy patients suffering from extrarespiratory symptoms (including skin, gastrointestinal, or flu-like symptoms) in relation to sensitized pollen exposure. Considering the systemic nature of allergic diseases, not only nasal/ocular symptoms but also extrarespiratory symptoms can be related to impaired quality of life and productivity for patients with pollen allergy. However, studies on the systemic manifestation of pollen allergy are relatively limited. The aim of this study was to elucidate extrarespiratory symptoms in patients with pollen allergy.

Method: This was a non-drug-focused prospective study. From April to May 2021, a total of 384 patients with pollen allergy, who were sensitized to ≥ 1 pollen(s) (specific IgE ≥ 0.70 Ua/mL), were recruited from three institutions across Japan, in addition to symptom-free subjects ($n = 54$) as a control. During the 1-year observational period (from June 2021 to May 2022), all the patients/subjects were asked to complete a weekly e-diary consisting of a set of questionnaires (e.g., VAS) assessing all symptoms they experienced on various organs in the past week. An association between seasonal pollen levels and seasonal increases in VAS scores was evaluated using a mixed-effects model for repeated measures. A k-means cluster analysis was

performed to identify a group of patients with severe pollen allergy experiencing stronger extrarespiratory symptoms.

Results: In patients sensitized to grass pollen or Betulaceae pollen, higher seasonal levels of these pollens were associated with higher VAS scores for headache, gastrointestinal symptoms, skin symptoms, and fatigue/feverish. A cluster analysis identified a group of severe pollen allergic patients with higher respiratory and extrarespiratory symptoms throughout the year ($n = 42$). This group was characterized by a higher frequency of comorbid food allergy, food-related anaphylaxis, and IgE sensitization to Bet v 1 and/or Phl p 12, as well as higher work productivity and activity impairment.

Conclusion: This 1-year survey was the first to uncover underrecognized systemic symptoms in patients with severe pollen allergy. More attention should be paid to the systemic manifestation of pollen allergies, considering its potential impact on quality of life and working productivity.

Conflicts of interest: This study was funded by Novartis Pharma K.K.

Flash talks on immunomodulation

000923 | Garadacimab prophylaxis improves quality of life in adult and adolescent patients with hereditary angioedema: Results from a multicentre Phase 3 study

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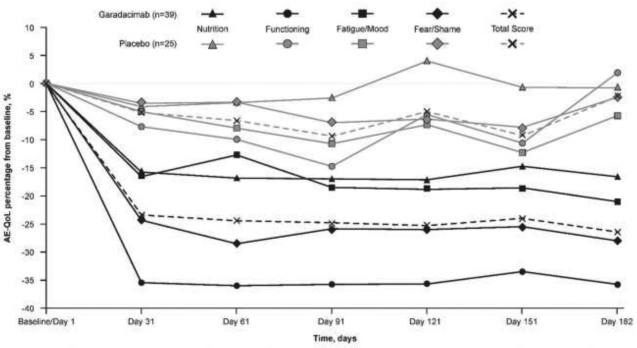
*Presenting author: P. Staubach

Background: Hereditary angioedema (HAE) is a rare, chronic and potentially life-threatening genetic disorder with recurrent swelling episodes affecting the skin, intestines and upper respiratory tract. These unpredictable symptoms negatively affect quality of life (QoL). Activated factor XII (FXIIa), an initiator of the contact system, produces bradykinin, a key mediator of HAE. Garadacimab, a first-in-class monoclonal antibody targeting FXIIa, significantly reduced the frequency of HAE attacks per month vs placebo (PBO; $p < 0.001$) in a Phase 3 randomised, double-blind, PBO-controlled, multicentre trial (VANGUARD, NCT04656418). Here, we report the QoL data from VANGUARD.

Method: Patients (Pts) aged ≥12 years with type I/II HAE ($n = 64$) were randomised (3:2) to receive a subcutaneous (SC) 400 mg loading dose followed by monthly SC 200 mg garadacimab or matching PBO for 6 months. QoL was evaluated using patient-reported outcomes, including the Subject Global Assessment of Response to Therapy (SGART; patients of all ages) and Angioedema Quality of Life Questionnaire (AE-QoL; adult patients). Logistic regression was used to compare proportions of patients achieving a clinically meaningful improvement in total AE-QoL score. A Mixed Model for Repeated Measures was used to test for a treatment effect.

Results: At Day 182, 31 Pts (81.6%) in the garadacimab arm responded 'good or better' in SGART vs eight Pts (33.0%) in the PBO arm ($p < 0.001$). Only one Pt (2.6%) in the garadacimab arm rated response to treatment as 'none' (indicating no or worsening response) in SGART vs 10 Pts (41.7%) in the PBO arm. A clinically meaningful improvement of at least 6 points in the AE-QoL total score was reported by 29/33 adult Pts (87.9%) in the garadacimab arm vs 11/20 Pts (55.0%) in the PBO arm (nominal $p = 0.004$). Garadacimab significantly improved AE-QoL total score vs PBO (nominal $p < 0.001$): AE-QoL total score was improved by −26.5 (95% CI: −32.8, −20.1) in the garadacimab arm from baseline to Day 182 (mean total score [SD]: 38.8 [15.0] vs 11.7 [15.6]) vs a change of −2.2 (95% CI: −11.2, 6.7) in the PBO arm (mean total score [SD]: 43.7 [21.4] vs 40.3 [24.1]). Similar trends were observed across domain scores (Figure 1).

Conclusion: Consistent with the demonstrated efficacy in preventing HAE attacks, once-monthly SC garadacimab prophylaxis improved QoL as shown by the improvement vs PBO in SGART response and mean AE-QoL total score after 6 months, with improvement across all AE-QoL domains.



Baseline mean score	Nutrition	Functioning	Fatigue/Mood	Fear/Shame	Total Score
Garadacimab 200 mg (n=39)	23.897	43.199	34.559	44.240	38.754
Placebo (n=25)	26.705	42.045	42.273	51.515	43.650

FIGURE 1 AE-QoL percentage change from baseline. AE-QoL, Angioedema Quality of Life Questionnaire.

Conflicts of interest: W. R. Lumry is a speaker for AstraZeneca, CSL Behring, Grifols, GSK, Optinose, Pharming, Sanofi/Regeneron and Takeda/Shire; has served as a consultant for Astria, BioCryst, BioMarin, CSL Behring, Fresenius Kabi, Intellia, KalVista, Pharming, Pharvaris and Takeda/Shire; is a board member of the US Hereditary

Angioedema Association Medical Advisory Board; and has received grants/research support from BioCryst, BioMarin, CSL Behring, Grifols, Ionis, KalVista, Takeda/Shire and Teva. M. Magerl has received financial support from CSL Behring for acting as a study-center investigator during the conduct of the study, and personal fees from BioCryst, CSL Behring, KalVista, Novartis, Octapharma, Pharming Technologies and Takeda/Shire outside the submitted work. T. J. Craig is a speaker for CSL Behring, Fresenius Kabi, Grifols, Pharming and Takeda; has received research and consultancy grants from BioCryst, BioMarin, CSL Behring, Fresenius Kabi, Grifols, Ionis, Spark and Takeda; is on the Medical Advisory Board for the US Hereditary Angioedema Association; is a Director of Angioedema Center of Reference and Excellence (ACARE), Penn State University, Hershey, PA, USA; and is on the Board of Directors for the American Academy of Allergy, Asthma, and Immunology (AAAAI). H. Farkas received research grants from CSL Behring, Pharming and Takeda; has served as an advisor for BioCryst, CSL Behring, KalVista, ONO Pharmaceutical, Pharming and Takeda; and has participated in clinical trials/registries for BioCryst, CSL Behring, KalVista, Pharming, Pharvaris and Takeda. W. H. Yang has been a speaker, advisory board member and has received honoraria from CSL Behring, Merck, Novartis, Sanofi Genzyme and Takeda/Shire; has received research grants from Aimmune, ALK Pharma, Amgen, AnaptysBio, AstraZeneca, BioCryst, Celgene, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Galderma, Genentech/Roche, Glenmark, GSK, Ionis, Novartis, Pharming, Pharvaris, Regeneron, Sanofi Genzyme and Takeda/Shire; serves as a medical advisor (volunteer) for HAE Canada, a patient organisation; and is a member of Angioedema Centers of Reference and Excellence (ACARE). E. S. G. Stroes has received lecturing/advisory board fees from Amgen, AstraZeneca, Esperion, Ionis/Akcea, Merck, Novartis and Sanofi, paid to the institution. I. Martinez Saguer has received honoraria, research funding and travel grants from BioCryst, CSL Behring, KalVista, Octapharma, Pharming and Takeda/Shire, and/or has served as a consultant and/or participated in advisory boards for these companies. E. Aygören-Pürsün has received honoraria as a speaker/advisor and/or grant support/clinical trial investigator support from Adverum Biotechnologies, BioCryst, BioMarin Europe, Centogene, CSL Behring, KalVista, Pharming Technologies, Pharvaris and Takeda/Shire. P. Staubach has received honoraria, research funding, travel grants and/or has served as a consultant and/or participated in advisory boards for CSL Behring, Octapharma, Pharming, Shire and Takeda. R. Treudler has received honoraria, travel grants and/or has participated in clinical trials and/or advisory boards for CSL Behring, Shire and Takeda. R. Itzler is a full-time employee and shareholder of CSL Behring. H. Feuersenger is a full-time employee and shareholder of CSL Behring. I. Pragst is a full-time employee and shareholder of CSL Behring. A. Reshef received research grants as a Principal Investigator, speaker and advisor for BioCryst, CSL Behring, Ionis, Pharming, Pharvaris, Shulov Innovative Science and Takeda/Shire.

000924 | Long-term efficacy and safety of subcutaneous garadacimab for prophylaxis of hereditary angioedema attacks: Results from a multicentre phase 3 study and open-label extension

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Background: Activated factor XII (FXIIa) is an initiator of the contact cascade, which produces bradykinin, a key mediator of hereditary angioedema (HAE). The safety and efficacy of garadacimab, a fully human monoclonal antibody targeting FXIIa for the prevention of HAE attacks, were evaluated in a pivotal, randomised, placebo-controlled, 6-month, multicentre, Phase 3 trial and an open-label extension (OLE) trial.

Method: Patients (Pts) aged ≥12 years with type I/II HAE ($n = 64$) were randomised (3:2) to receive monthly subcutaneous (SC) garadacimab 200 mg ($n = 39$) or placebo ($n = 25$, PBO) for 6 months after an initial 400 mg SC loading dose or matched PBO. Pts completing the pivotal Phase 3 trial could enrol into the OLE. Primary and key secondary endpoints of the Phase 3 trial and the long-term efficacy and safety of garadacimab in Pts who rolled over into the OLE ($n = 57$) are reported.

Results: In the 6-month Phase 3 trial, garadacimab significantly reduced mean number of investigator-confirmed HAE attacks per month (0.27, 95% confidence interval [CI] 0.05, 0.49) vs PBO (2.01, 95% CI, 1.44, 2.57; $p < 0.001$). Reduction in least squares

mean monthly attack rate was −89.2% (95% CI −95.2, −75.6). Of garadacimab-treated Pts, 24 (61.5%) were attack-free and 29 (74.4%) achieved ≥90% attack reduction vs run-in period; no patients in PBO arm were attack-free and 2 (8.3%) achieved ≥90% attack reduction vs run-in period. Interim OLE data (as of 30 Sept 2022) of Pts who rolled over show that efficacy of garadacimab ($n = 36$) was sustained; mean (median) reduction in time-normalised number of HAE attacks was −95.8% ([−100.0%] 95% CI −100.0, −91.6) vs run-in period. Previously PBO-treated Pts receiving garadacimab ($n = 21$) in the OLE had a mean (median) reduction in number of HAE attacks of −92.6% ([−100.0%] 95% CI −99.3, −85.8) vs run-in period. In the Phase 3 trial, safety profiles of garadacimab and PBO were similar. Upper-respiratory tract infections, nasopharyngitis and headaches were the most common adverse events (AEs) across treatments. No deaths, bleeding or thrombotic events, or treatment discontinuations due to AEs were observed. In the OLE, safety profiles were consistent with Phase 3 trial data (Table 1).

Conclusion: Once-monthly SC garadacimab substantially reduced the number of HAE attacks vs PBO with early onset of protection from first dose, sustained efficacy beyond 12 months, and a favourable safety profile. Efficacy in the OLE was comparible between Pts previously treated with garadacimab or PBO.

	Phase 3 Study N=64				OLE Study N=57			
Type of event	Garadacimab (n=39)		PBO (n=25)		Garadacimab recieved in Phase 3 trial and OLE 200 mg (n=36)		PBO recieved in Phase 3 trial and garadacimab in OLE (n=21)	
	n (%)	E	n (%)	E	n (%)	E	n (%)	E
Total TEAEs	25 (64.1)	75	15 (60.0)	54	27 (75.0)	61	14 (66.7)	52
Related to treatment	4 (10.3)	9	3 (12.0)	5	2 (5.6)	2	4 (19.0)	15
ISR	2 (5.1)	3	3 (12.0)	3	2 (5.6)	2	4 (19.0)	13
Headache	3 (7.7)	9	4 (16.0)	4	0	0	1 (4.8)	1
Thromboembolic or bleeding event*	0	0	0	0	0	0	0	0
Leading to study discontinuation	0	0	0	0	0	0	0	0
Serious AEs	1 (2.6)**	1	0	0	0	0		
AESIs	0	0	0	0	0	0	0	0
Death	0	0	0	0	0	0	0	0

TABLE 1 Overview of AEs in the OLE study in patients who rolled over from the pivotal Phase 3 trial

*There were no thromboembolic or bleeding events, only 'intermenstrual bleeding' and 'heavy menstrual bleeding' were reported as bleeding events. **One severe serious AE (laryngeal attack) assessed as not related to trial treatment: the patient made a full recovery after being hospitalized and being kept under observation overnight
AE, adverse event; AESI, adverse event of special interest; ISR, injection site reaction; n, number of subjects with at least 1 event; E, number of events; OLE, open-label extension; PBO, Placebo; TEAE, treatment-emergent adverse event

Conflicts of interest: M. Magerl has received financial support from CSL Behring for acting as a study centre investigator during the conduct of the study and personal fees from BioCryst, CSL Behring, KalVista, Novartis, Octapharma, Pharming Technologies and Takeda/Shire outside the submitted work.A. Reshef received research grants as a principal investigator, speaker and advisor for BioCryst, CSL Behring, Ionis, Pharming, Pharvaris, Shulov Innovative Science and Takeda/Shire. H. Farkas received research grants from CSL Behring, Pharming and Takeda; has served as an advisor for BioCryst, CSL Behring, KalVista, ONO Pharmaceutical, Pharming and Takeda; and has participated in clinical trials/registries for BioCryst, CSL Behring, KalVista, Pharming, Pharvaris and Takeda.H. H. Li is a speaker for BioCryst, CSL Behring, Pharming and Takeda; and has received research and consultancy grants from BioCryst, BioMarin, CSL Behring, Ionis, Pharming, Phavaris and Takeda.J. S. Jacobs is a speaker for AstraZeneca, CSL Behring, GSK, Regeneron, Sanofi Genzyme, Takeda/Shire and Teva; and has received research funding/consultancy fees from Allakos, AstraZeneca, Astria, BioCryst, CSL Behring, Fresenius Kabi, Genentech, GSK, Pharvaris, Novartis, Regeneron and Takeda/Shire.J. A. Bernstein is a consultant, principal investigator and speaker for BioCryst, CSL Behring, Pharming and Takeda/Shire; is a consultant/principal investigator for Biomarin, Ionis and KalVista; and is a consultant for Astria, Cycle, ONO and Pharvaris.W. H. Yang has been a speaker, advisory board member and has received honoraria from CSL Behring, Merck, Novartis, Sanofi Genzyme and Takeda/Shire; has received research grants from Aimmune, ALK Pharma, Amgen, AnaptysBio, AstraZeneca, BioCryst, Celgene, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Galderma, Genentech/Roche, Glenmark, GSK, Ionis, Novartis, Pharming, Pharvaris, Regeneron, Sanofi Genzyme and Takeda/Shire; serves as a medical advisor (volunteer) for Hereditary Angioedema Canada, a patient organization; and is a member of Angioedema Centers of Reference and Excellence.E. S. G. Stroes has received lecturing/advisory board fees from Amgen, AstraZeneca, Esperion, Ionis/Akcea, Merck, Novartis and Sanofi, paid to the institution.I. Ohsawa has received honoraria and/or has served as a consultant and/or participated in advisory boards for CSL Behring, Takeda/Shire and Torii Pharmaceutical Company Ltd. R. Tachdjian is a speaker for AstraZeneca, BioCryst, CSL Behring, GSK, Pharming, Sanofi/Regeneron and Takeda; has served as a consultant for BioCryst, CSL Behring, KalVista, Pharming and Takeda; and has received grants/research support from BioCryst, CSL Behring, Ionis, KalVista, Pharvaris and Takeda.M. E. Manning is a speaker for Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Genentech, GSK, Pharming, Sanofi/Regeneron and Takeda; has received research grants from Allakos, BioCryst, CSL Behring, GSK, KalVista, Merck, Novartis, Pharming, Pharvaris and Takeda; and has served as a consultant for BioCryst, CSL Behring, Cycle, KalVista, Pharming and Takeda.W. R. Lumry is a speaker for AstraZeneca, CSL Behring, GSK, Pharming, Sanofi/Regeneron and Takeda/Shire; has served as a consultant for BioCryst, BioMarin, CSL Behring, Fresenius Kabi, Intellia, KalVista, Pharming, Pharvaris and Takeda/Shire; is a board member of the US Hereditary Angioedema Association Medical Advisory Board; and has received grants/research support from ALK, BioCryst, CSL Behring, Ionis, Gossamer, KalVista, Kedrion, Takeda/Shire and Therapure.I. Martinez Saguer has received honoraria, research funding and

travel grants from BioCryst, CSL Behring, KalVista, Octapharma, Pharming and Takeda/Shire, and/or has served as a consultant and/or participated in advisory boards for these companies.E. Aygören-Pürsün has received honoraria as a speaker/advisor and/or grant support/clinical trial investigator support from Adverum Biotechnologies, BioCryst, BioMarin Europe, Centogene, CSL Behring, KalVista, Pharming Technologies, Pharvaris and Takeda/Shire.B. Ritchie has been a speaker and advisory board member for CSL Behring and Takeda, but has not received personal reimbursement for these activities; has participated in multiple clinical trials involving investigational drugs for BioCryst, CSL Behring, Dyax, Pharming and Takeda (he does not hold patents or investments with these companies or involving this product); and serves as a volunteer medical scientific advisor to HAE Canada, a patient organization.G. L. Sussman has been an advisory board member for CSL Behring and has participated in clinical trials for investigational drugs for BioCryst, CSL Behring, Dyax, KalVista, Pharming, Pharvaris and Takeda.J. Anderson is a speaker bureau member for BioCryst, CSL Behring, Pharming and Takeda; has received consulting fees from and is a clinical trial investigator for BioCryst, BioMarin, CSL Behring, KalVista, Pharming, Pharvaris and Takeda; and has received consulting fees from Cycle.K. Kawahata has not received any consulting fees, honoraria or grants; is not a shareholder of any pharmaceutical company; and has been a clinical trial investigator for CSL Behring.Y. Suzuki has received speaker fees from AstraZeneca, Novartis, Takeda/Shire and Torii Pharmaceutical Company Ltd; and has been a clinical trial investigator for CSL Behring.P. Staubach has received honoraria, research funding, travel grants and/or has served as a consultant and/or participated in advisory boards for CSL Behring, Octapharma, Pharming and Takeda.R. Treudler has received honoraria, travel grants and/or has participated in clinical trials and/or advisory boards for CSL Behring and Takeda.H. Feuersenger is a full-time employee and shareholder of CSL Behring.I. Jacobs is a full-time employee and shareholder of CSL Behring.T. J. Craig is a speaker for CSL Behring, Fresenius Kabi, Grifols, Pharming and Takeda; has received research and consultancy grants from BioCryst, BioMarin, CSL Behring, Fresenius Kabi, Grifols, Ionis, Spark and Takeda and is on the Medical Advisory Board for the HAE-A, Director of ACARE Angioedema Center at Penn State University, Hershey, PA, USA; and is on the Board of Directors for the AAAAI.

001422 | Immune-modulatory effects of dietary fiber pectin supplementation in a peanut experimental mouse model

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Background: Pectin (a heteropolysaccharide accumulating in cell walls and intracellular regions of higher plants) is widely used in food industry as thickening and gelling agent. This dietary fiber can be classified according to the degree of esterification (DE) as high methoxyl (HMP; DE>50%) or low methoxyl pectin (LMP; DE<50%). Pectins are prebiotics which exert immune-modulatory properties, comprising direct effects on immune cells and indirect effects mediated by bacterial metabolites upon fermentation in the gut. Nevertheless, distinct effects associated with different pectin structures is still unclear. An own previous study showed that HMP pectin supplementation promotes a shift towards *Bacteroides*, a beneficial bacteria and producer of SCFA. This study aimed to evaluate the effect of HMP and LMP supplementation on a peanut allergy mouse model, examining humoral, local immune response and gut microbiota.

Method: CBA/J mice were sensitized weekly 4-times intragastrically with an extract from roasted peanuts using cholera toxin as adjuvant, and challenged intraperitoneally one week after the last sensitization with recombinant Ara h 2. Mice were fed a diet containing 15% pectin and 5% cellulose one week before sensitization until challenge. Peanut allergic (positive control) and PBS-treated (negative control) mice were fed a 20% cellulose diet. Feces and serum were subjected to microbiota and immunological analysis, respectively. Immune cells of lamina propria (LP) were analyzed via FACS.

Results: HMP rather than LMP supplementation promoted a reduced body core temperature drop after challenge. Both pectins induced the enlargement of small, large intestine and caecum size, increased frequency of CD4+ Tcells, but reduced number of CD8+ and Tcells in the LP of the large intestine. Although the number of mast cells remained unchanged, the activation status, measured as mMCPT-1 levels, was reduced. Moreover, HMP supplementation promoted decreased peanut-specific IgE, IgG1 and IgG2a values in sera and a reduced frequency of immune cells as eosinophils, macrophages and dendritic cells in the LP. Microbiota analysis will be performed.

Conclusion: Pectin supplementation modulated the immune response in allergic mice. Particularly, HMP reduced signs of Th2 immune responses in a preventive supplementation experimental setting. Suggesting that pectins with a higher DE may have stronger immune-modulatory effects promoting the tolerance in allergic mice.

Conflicts of interest: The authors did not specify any links of interest.

001480 | Mouse-specific IgG4 antibodies and clinical tolerance to laboratory animal allergy in a modern animal research setting

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Background: Occupational exposure to rodents is a major risk factor for laboratory animal allergy (LAA) and is associated with the development of rodent-specific IgE and IgG4 antibodies. However, the exposure-response relationship is still not well understood. Specific IgG4 may play a role in the induction of clinical tolerance to LAA, but findings from previous studies on specific-IgG4 have been inconsistent. In this work, we aimed to investigate the associations between mouse-specific antibodies (IgE and IgG4), mouse exposure, and clinical tolerance to LAA in a modern animal research setting.

Method: Allergic symptoms and occupational mouse exposures were measured in a cross-sectional study of laboratory animal workers from seven UK research institutions. Serum samples were tested for the presence of mouse-specific IgE and IgG4 ($n = 612$) using commercial and in-house enzyme-linked immunosorbent assay's (ELISA's). The capacity of IgG4 to inhibit allergen-IgE complex binding to B-cells was measured in a subset ($n = 86$) of workers using the IgE-Facilitated Antigen Binding (IgE-FAB) assay.

Results: Levels of mouse-specific IgG4 were associated with increased exposure to mice and with job title ($p < 0.001$). After adjusting for confounders, both IgE and IgG4 were associated with reporting of at least one work-related symptom. When restricting the same analysis to workers with IgE sensitisation to mice, those reporting work-related asthma symptoms had significantly lower specific-IgG4 levels than those without asthma symptoms (geometric mean ratio 0.32, 95%CI: 0.12–0.83). Inhibition of allergen-IgE complex binding to CD23-expressing B cells was greater in workers with the highest levels of specific-IgG4 (72.6%, IQR: 49.1%–87.8%) compared with workers with specific-IgG4 levels below the ELISA's limit of detection (13.8%, IQR: 4.5%–44.9%) ($p < 0.001$).

Conclusion: Higher levels of mouse exposure in animal research facilities were associated with increased levels of mouse-urine specific IgG4 antibodies in laboratory animal workers. In our population, animal workers who were sensitised to mice but did not have work-related asthma symptoms had significantly higher levels of mouse specific IgG4 compared to sensitised workers with work-related asthma symptoms. This suggests that mouse-specific IgG4 may play a role in clinical tolerance to LAA, and its mechanism may be through the inhibition of IgE-allergen complex binding to B cells.

Conflicts of interest: The authors did not specify any links of interest.

001628 | Specific human milk oligosaccharides differentially promote Th1 and regulatory responses in CpG-activated epithelial/immune cell coculture

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Background: Proper early life immune development creates a basis for a healthy and resilient immune system, which balances immune tolerance and activation. Deviations in immune maturation can have life-long effects, such as development of allergic diseases. Evidence suggests that human milk oligosaccharides (HMOS) possess immunomodulatory properties essential for neonatal immune development. HMOS are known to modulate the microbiome, less is known about their direct effects in modulating the function of intestinal epithelial cells (IEC) and/or immune cells. The aim of these studies is to identify the immunomodulatory properties of enzymatic or bacterial produced HMOS, the effects of five HMOS (2'FL, 3FL, 3'SL, 6'SL and LNnT) present in human milk were studied.

Method: A human PBMC immune model, IEC (T84 cells) barrier model and IEC (HT-29 cells)/PBMC transwell coculture model were used, representing critical steps in mucosal immune development. HMOS were applied to PBMC, IEC or IEC in coculture with activated PBMC.

Results: The HMOS differentially promoted either Th1 type IFNγ ($p < 0.001$) and/or regulatory IL10 ($p < 0.0001$) secretion when added to activated PBMC. The HMOS did not prevent type 2 cytokine mediated epithelial barrier disruption. In the IEC/PBMC coculture however, in the presence of CpG (bacterial DNA mimic), apical exposure of 2'FL or 3FL to IEC, enhanced IFNγ ($p < 0.01$), IL10 ($p < 0.0001$) and galectin-9 ($p < 0.001$) secretion by IEC and/or PBMC as measured in the basolateral compartment. 2'FL as well as 3FL decreased Th2 cell development, while 3FL enhanced Treg polarization ($p < 0.05$). IEC were required for this 3FL mediated Treg polarization, which was not explained by epithelial-derived galectin-9, TGFβ nor retinoic acid secretion.

Conclusion: The most pronounced immunomodulatory effects, linking to enhanced type 1 and regulatory mediator secretion, were observed for 2'FL and 3FL. Future studies are needed to further understand the complex interplay between HMOS and early life mucosal immune development.

Conflicts of interest: The division of Pharmacology at Utrecht University collaborates within a strategic alliance with Danone Nutricia ResearchJ. Garssen is advisor at Danone-Nutricia Research B.V.B. van't Land is employee at Danone-Nutricia Research B.V.

001207 | Iron homeostasis differ in dogs suffering from canine atopic dermatitis from non-allergic dogs

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Background: In humans, dysbalanced iron homeostasis is linked to allergic diseases. We have shown that allergics suffer from functional iron-deficiency and that their iron homeostasis differs from non-atopic individuals. Here, we aimed to establish whether also in dogs iron parameters are skewed when suffering from Canine Atopic Dermatitis (CAD) compared to non-allergic, healthy dogs.

Method: For this retrospective study, sera of 36 dogs with confirmed CAD an on immunosuppressive medication were compared with 102 healthy non-atopic dogs, in which blood were obtained after fasting. The parameters accessed were Total Iron, total iron binding capacity TIBC, UIBC; hepcidin, transferrin, ceruloplasmin as a marker for mobilizing cellular iron stores, ferritin and hs-CRP.

Results: Allergic dogs had significantly higher serum iron concentration than non-allergic dogs ($p = 0.012$), and this positively correlated with ceruloplasmin levels and negatively with CRP levels.

In contrast, in the cohort of healthy dogs' values for UIBC, Hepcidin, ceruloplasmin concentrations were significantly (all $p < 0.001$) higher and serum iron was positively associated with ferritin levels and negatively with hepcidin-levels.

Conclusion: Iron homeostasis [MOU1] differed between healthy dogs and those suffering from canine atopic dermatitis. In CAD patients, but not healthy dogs, serum iron dependent on inflammatory markers such as CRP and ceruloplasmin suggesting an involvement of iron in the etiology.

Conflicts of interest: F.R.-W and E.J.J are inventors of EP2894478 (Roth-Walter F et al., Method and means for diagnosing and treating allergy.) (applicant Biomedical International R+D GmbH, Vienna, Austria). F.R.-W. received research funding from Biomedical International R+D GmbH, Vienna, Austria, Bencard Allergie GmbH, Munich, Germany and Vienna, Austria, and Allergy Therapeutics, Worthing, UK. Moreover, F.R.-W rand E.J.J. eceived lecture honoraria by Bencard Allergie GmbH, Munich, Germany and Vienna, Austria, and Allergy Therapeutics, Worthing, UK. The other authors declare no relevant conflict of interest in relation to this abstract

000159 | MY006: A passive immunotherapy for the treatment of peanut allergy

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Background: Peanut allergy is one of the most common food allergies, with some of the highest rates of severe reactions including fatal anaphylaxis. Complete allergen avoidance is challenging, leaving a constant threat of anaphylaxis due to accidental peanut encounter. Allergen-specific oral immunotherapy is currently the only treatment option.

Method: Mabylon has developed MY006, a cocktail of anti-peanut antibodies by exploiting its human antibody discovery pipeline for cloning peanut allergen-specific human antibodies from allergic patients. After screening our human-derived peanut antibody library, we selected the most potent antibody cocktail.

Results: The engineered antibodies are binding the major peanut allergens with high affinity and show an excellent developability profile. MY006 inhibits patients' IgE binding to peanut allergens and prevents basophil activation and degranulation from peanut allergic patients. In addition, treatment of mice with a single dose of MY006 prevents anaphylactic reactions upon peanut challenge in an actively sensitized mouse model as well as in a passively sensitized humanized mouse model of peanut allergy.

Conclusion: In conclusion, MY006 holds great promise as a novel therapy for peanut allergy, with a predicted immediate onset of protection and good safety profile. Two different therapeutic applications are investigated: (i) A passive immunotherapy with MY006 and ii) a combination of active allergen immunotherapy and passive MY006 immunotherapy, which may accelerate and improve the safety and efficacy of peanut immunotherapy.

Conflicts of interest: The authors did not specify any links of interest.

000161 | MY010: A passive immunotherapy for the treatment of birch pollen allergy

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*Presenting author: C. Arena

Background: The prevalence of pollen allergies is up to 30% in industrialized countries with more than 100M people suffering from

birch pollen allergies worldwide. Clinical manifestations include allergic rhinoconjunctivitis, asthma as well as pollen-related food allergy syndrome. Management of pollen allergies are symptomatic treatments (oral steroids, β-agonists, antihistamines) and subcutaneous/ sublingual allergen immunotherapy. Limitations of the latter are lengthy and cumbersome treatments requiring high patient compliance, adverse reactions and a variable efficacy.

Method: Mabylon has developed a human antibody discovery pipeline that allowed us to clone and express Bet v 1-specific recombinant human antibodies from allergic patients. Human-derived antibodies are targeting disease-relevant proteins and epitopes, allowing quick translation and low development attrition.

Results: After screening our human-derived anti-birch antibody library, we selected the most potent antibody cocktail, MY010, to develop as a passive immunotherapy for the treatment of birch-related pollen allergies. The antibodies are binding Bet v 1 with high affinity and show broad cross-reactivity to homologous Bet v 1 allergens. MY010 inhibits patients' IgE binding to the allergens and prevents basophil activation and degranulation upon allergen challenge, both in sensitized basophils and in whole blood assays from allergic patients. In addition, treatment of mice with a single dose of MY010 prevents allergic reactions in a passively sensitized humanized mouse model of pollen allergy.

Conclusion: In conclusion, MY010 holds great promise as a novel therapy for birch-related pollen allergy, with a predicted immediate onset of protection and good safety profile. Mabylon has applied the same human antibody discovery pipeline to develop passive immunotherapy for peanut and grass pollen allergy.

Conflicts of interest: The authors did not specify any links of interest.

100235 | The protective effect of raw cow's milk in allergy can be explained by the presence of high levels of aeroallergen-specific IgGs

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Background: Over the last 20 years, evidence has been accumulating that growing up on a farm is associated with a decreased prevalence of asthma and rhinitis. This effect is linked to the consumption of unprocessed raw cow's milk and to microbial exposure. The effect of farm milk consumption is only seen when the farm milk is not heated, suggesting that it is linked to the presence of non-denatured milk proteins. Cow's milk contains immune regulatory components such as immunoglobulins, especially IgG, lactoferrin, TGF-β.

Hypothesis: Allergen-specific IgGs in unprocessed milk consumed at farms is present for the most common aeroallergens and these sIgGs can block allergen-mediated activation of effector cells as well as CD23-mediated facilitated antigen presentation.

Aim: The presence of aeroallergen-specific IgGs was determined in colostrum, unprocessed milk, pasteurized milk and sterilized milk. The functional effects of these IgGs will be tested on the binding of house dust mite (HDM)-IgE immune complexes to CD23-expressing B cells, as well as their blocking effects in HDM-induced basophil activation in BAT.

Method: The presence of IgG was determined in different unprocessed and processed cow's milk products by the EUROLINE inhalation membrane strips (EUROIMMUN AG) and alkaline phosphatase-labeled anti-bovine IgG The binding of immune complexes of serum IgE with house dust mite allergens (ALK, Denmark) to CD23-expressing B cells was determined using flow cytometry.

Results: In colostrum, raw milk products and commercially available pasteurized cow's milk IgGs were present in high amounts against the mites *D. farinae*, *D. pteronyssinus*, the fungi *A. alternata*, *A. fumigatus*, *C. herbarum* and *P. notatum*, sweet vernal, orchard, timothy and cultivated rye grasses, hazel tree pollen and ragweed. Some moderate sIgG levels were found for alder, birch and oak tree pollen and mugwort and English plantain. No sIgG were detected for cat, dog or horse allergens. The highest level for sIgG was demonstrated in colostrum. The sIgG level in raw milk differed between different farms but was comparable to that found in pasteurized cow's milk. Commercially available sterilized (Ultra-high temperature treated) cow's milk was completely missing any sIgGs for the aeroallergens tested. The binding of house dust mite-IgE complexes was shown for 5 HDM allergic donors. Although values were generally slightly lower, preincubation with bovine IgG had no significant blocking effect on the binding of IgE immune complexes to CD23-expressing B cells.

Conclusion: Cow's milk contains significant levels of IgGs against the most common aeroallergens, which are lost after sterilization. This might explain the decreased allergy prevalence associated with raw milk consumption. Even though these do not compete significantly with allergen-specific IgE, they are known to bind to human FcgRII and may have immunomodulatory effects yet to be explored. Further studies will examine the functional properties of these allergen-specific IgGs in blocking allergen-mediated basophil activation.

Conflicts of interest: The authors did not specify any links of interest.

001408 | Household laundry detergents disrupt barrier integrity and induce inflammation in mouse and human skin

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*Presenting author: Y. Mitamura

Background: The impairment of the epithelial barrier function is associated with various skin allergic and inflammatory disorders.

Laundry detergents have been demonstrated to induce epithelial barrier dysfunction *in vitro* using with air-liquid interface cultures of human epithelial cells. Our group previously demonstrated that electrical impedance spectroscopy (EIS) is the noninvasive tool to detect skin barrier function *in vivo*. *Ex-vivo* experiments with human skin (NativeSkin®) is a model that exhibits normal skin barrier function and contains almost all cell types.

Method: Back skin of C57BL/6 mice was treated with two household laundry detergents at several dilutions (1:100, 1:1,000, 1:10,000). Skin barrier function was assessed by EIS and transepidermal water loss (TEWL) measurements after the 4 hours treatments with detergents. RNA-seq from skin biopsies and targeted multiplex proteomics analyses in skin lysate samples were performed. The effect of laundry detergent and its main component sodium dodecyl sulfate (SDS) were investigated on NativeSkin.

Results: The epicutaneous application of different dilutions of household laundry detergents led to a significant decrease in skin barrier function *in vivo*. Both TEWL and EIS showed the skin barrier dysfunction, with a relatively higher sensitivity and dose response in EIS. The topical application of the two detergents substantially reduced the expression of several genes essential for skin barrier integrity, such as TJs transmembrane proteins. In contrast, keratinization, lipid metabolic processes, epidermal cell differentiation and epidermis development were upregulated. Proteomics analysis showed that the detergents generally downregulated cell adhesion molecules 24 hours after their application. Cell adhesion-related proteins, such as ITGB6 and CNTN1 were downregulated and inflammatory proteins, such as IL6 and CCL2 were upregulated by the treatment. Both detergent and SDS led to a significant decrease ın EIS values in our *ex-vivo* human skin model.

Conclusion: In conclusion, the present study shows that household laundry detergents can disrupt the skin barrier, even when highly diluted and exposed only for 4 hours in mouse skin. Laundry detergents and SDS caused a barrier damage in human skin as well. Our findings suggest that the daily exposure to detergents may cause skin barrier disruption and play a role in the development of chronic inflammatory skin diseases.

Conflicts of interest: AR and CA report a patent application on "Methods and medical devices for analyzing epithelial barrier function". BJ, ALN, LR declare receiving personal fees from SciBase AB. GN declare receiving personal fees from Genoskin SAS. CA has received research grants from the Swiss National Science Foundation, European Union (EU CURE, EU Syn-Air-G), Novartis Research Institutes, (Basel, Switzerland), Stanford University (Redwood City, Calif), and SciBase (Stockholm, Sweden); is the Co-Chair for EAACI Guidelines on Environmental Science in Allergic diseases and Asthma; is on the Advisory Boards of Sanofi/Regeneron (Bern, Switzerland, New York, USA), Stanford University Sean Parker Asthma Allergy Center (CA, USA), Novartis (Basel, Switzerland), Glaxo Smith Kline (Zurich, Switzerland), Bristol-Myers Squibb (New York, USA), Seed Health (Boston, USA) and SciBase (Stockholm, Sweden); and is the Editor-in- Chief of Allergy

Flash talks on allergy diagnosis II

000677 | Association between IgE levels to dog dander extract and sensitization profiles to dog molecular allergens

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*Presenting author: S.S. Ozuygur Ermis

Background: While component resolved-diagnostics (CRD) is improving the diagnosis of allergy to furry animals, whole extract-based analysis of serum Immunoglobulin E (IgE) remains the first step in the diagnostic workup. We aimed to examine the cut-off values of dog dander extract levels in identifying IgE sensitization profiles to dog molecular allergens.

Method: The data was collected from a representative cohort, the West Sweden Asthma Study. Subjects who tested positive for dog dander extract (≥ 0.35 kUA/L) were included in the study and then analysed for dog molecular allergens (Can f 1-6). IgE levels ≥ 0.35 kUA/L were the threshold for positivity to single allergens. We subcategorized sensitization patterns according to the current diagnostic algorithm: (i) primary sensitization to dog (at least one of Can f 1/2/4/5[+] and Can f 3/6[−]); (ii) *primary* sensitization to dog with probable co- or cross-sensitization to other furry animals (at least one of Can f 1/2/4/5[+] and at least one of Can f 3/6 [+]); and (iii) *the* component negative group without any sensitization to dog molecular allergens. Receiver operating characteristics (ROC) curves were drawn to calculate the area under curve (AUC) values for dog dander extract.

Results: AUC value was highest (AUC = 0.873, 95% CI = 0.83–0.92, $p < 0.001$) for primary sensitization with possible co- or cross-sensitization group, indicating IgE levels higher than 2.729 kUA/L shows a good discriminatory value (sensitivity = 79% and specificity = 81%). On the other hand, ROC curve failed to distinguish the primary sensitization to dog (AUC = 0.510, 95% CI = 0.45–0.57, $p = 0.779$). Of 313, 95 subjects were classified as component negative group. IgE levels < 0.860 kUA/L (AUC = 0.848, 95% CI = 0.80–0.89, $p < 0.001$) was the cut-off to identify the component negative group (sensitivity = 86% and specificity = 73%).

Conclusion: IgE levels to the whole dog extract gave discriminant cut-off values for primary sensitization to dog with possible co- or cross-sensitization, indicating the requirement of further analyses for the potential source of co- or cross-sensitization. Additionally,

IgE levels less than 0.860 kUA/L against whole extract could be helpful to distinguish the component negative group.

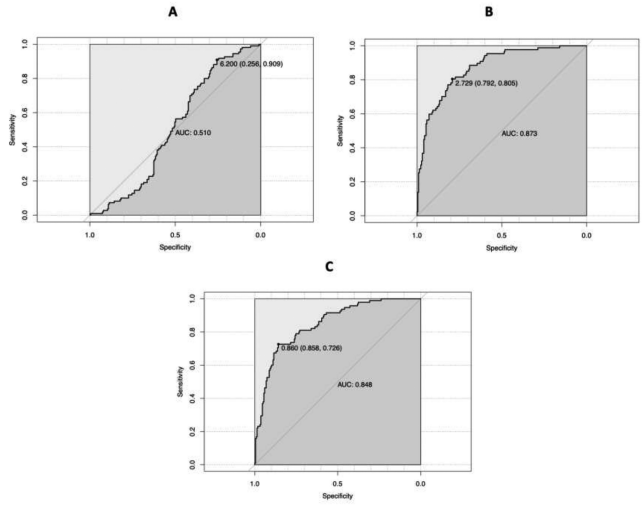

FIGURE 1 ROC curves for IgE levels to dog dander extract and sensitization profiles to dog molecular allergens. Groups were compared with the rest of the sample. AUC value was not significant for A) Primary sensitization to dog ($n = 110$). Optimal cut-off value was >2.729 kUA/L for (B) Primary sensitization to dog with possible co- or cross-sensitization to other furry animals ($n = 87$); < 0.860 kUA/L for (C) Component negative group ($n = 95$).

Conflicts of interest: M.P. Borres is employed by Thermo Fisher Scientific (Uppsala, Sweden). B. Nwaru have received material from Thermo Fisher to perform the IgE analyses for this work. H. Kankaanranta reports fees for consultancies and lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma and SanofiGenzyme outside the current study. The rest of the authors declare that they have no relevant conflicts of interest related to this work.

001072 | Basophil activation test in the diagnostic work-up of egg allergy: A real-life study

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*Presenting author: E. D'Auria

Background: The gold standard for diagnosing egg allergy in children is the oral food challenge (OFC). However, OFCs are time-consuming and risky procedures. Our study aimed to evaluate the clinical utility of the basophil activation test (BAT) in the diagnostic work-up of children with egg allergy.

Method: 86 children aged six months to 17 years, suspected of egg allergy, underwent OFC with boiled egg according to international standardized protocols. IgE testing to component egg proteins (Gal d 1-4) and BAT were also performed.

Results: BAT was performed in samples obtained by 75 of the 86 patients of our cohort. Egg white and yolk protein extracts induced a remarkable CD63 upregulation in the egg-allergic children compared with sensitized children that tolerated boiled egg (we registered an overall mean of CD63 expression in the egg-allergic population of 44.4% (SD 34.1) for egg white and 34.7% (SD 31.3) for egg yolk vs. 12.5% (SD 19.1) and 10.0% (SD 16.0) in sensitized children).BAT could discriminate between true egg allergy and egg sensitization in our population. In addition, the positivity of both Gal d 1 IgE and BAT were a hallmark of a true allergy, with only one false positive, and resulted in a sensitive reduction of the OFCs with a positive outcome ranging from 53% to 76%.

Conclusion: The BAT proved to be a useful diagnostic tool, in differentiating egg allergic from tolerant children, and in a stepwise approach combined with IgE for Gal d 1, to predict the allergic status and reduce the number of positive OFCs in children with egg allergy.

Conflicts of interest: The authors did not specify any links of interest.

001399 | Diagnostic accuracy of cereal-specific sIgE in flour-induced occupational asthma

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Background: Cereals flours are still the most prevalent cause of occupational asthma (OA) in Europe, accounting for about 30% of OA cases. The diagnosis of flour induced OA is complicated by the fact that skin prick tests with flours are not standardized and there is little information on the diagnostic efficiency of specific IgE (sIgE) against cereals.

We aim to evaluate the accuracy of wheat and rye sIgE in cereals flour induced OA.

Method: We retrospectively analyzed data from 184 subjects with suspected OA who completed a specific inhalation challenge (SIC) with flour in 2 tertiary centers (Strasbourg and Yvoir). The SIC was positive (i.e., ≥15% FEV1 fall) in 137 subjects. Receiver operating characteristics (ROC) analyses were conducted in order to determine the sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values of sIgE antibodies against wheat and rye compared to the result of the SIC with flour.

Results: Most of subjects (89%) were males and the median age was 38 years. Atopy was present in 66% of subjects and most of them

(91%) reported rhinitis at work. Based on the ROC curves, the optimal threshold for wheat-sIgE was 0.5 kUA/L. This threshold provided Se, Sp, PPV, and NPV of 83%, 77%, 91% and 61%, respectively. The optimal threshold value for rye-sIgE (i.e., 0.4 k UA/L) yielded Se, Sp, PPV, and NPV of 86%, 81%, 93% and 67%. Increasing the sIgE threshold value to 3.0 kUA/L for wheat and to 4.1 kUA/L for rye provided specificities and PPVs above 95%, but with low NPVs (i.e. 42% for wheat and 40% for rye).

Conclusion: High levels of wheat and rye sIgE antibodies exhibit excellent PPVs compared to the SIC with flour and allow for establishing a diagnosis of flour-induced OA with a high level of confidence while the NPVs are low

Conflicts of interest: The authors did not specify any links of interest.

000227 | Influence of *Lepidoglyphus destructor* sensitization on the clinical profile of patients allergic to mites and the overall molecular sensitization profiles in the Balearic Islands

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Background: Mites are the main source of perennial allergens worldwide with a great impact on developing allergic rhinoconjunctivitis, asthma and atopic dermatitis. In the Balearic Islands, the rate of sensitization to mites (66.7%) among patients who described allergic symptoms, is higher than the 43.2% of the national average.

Objective: To establish the influence of sensitization to *Lepidoglyphus destructor* on the clinical profile of patients allergic to mites in the Balearic Islands, determine the profile of molecular serodominance and cross-reactivity between group 2 allergens: *D. pteronyssinus* (Dpt) and *L. destructor* (Ldt).

Method: A molecular study was carried out using array images based on nanotechnology. This specific molecular panel (MADx) for 300 allergens was correlated with clinical parameters in 100 prick-tested patients allergic (rhinitis and/or asma) to dust mites in the Balearic Islands. Monoplex ImmunoCAP (ThermoFisher) was used to determine sIgE to Dpt and Ldt extracts. The GNU PSPP program (version 1.2.0-g0fb4db) was used for the statistical analysis of the data.

Results: 100 patients (65% women, 35% men) met the inclusion criteria, 100% had allergic rhinitis, 58% allergic asthma and 55% atopic dermatitis.

All of the patients had a positive prick test to Dpt, 48% to Dpt and Ldt. The whole sample showed specific IgE against Dpt and 51% to Dpt and Ldt.

93% of the patients recognized Der p 1 (sIgE average: 6.5 kU/L), 84% Der p 2 (20.8 kU/L), 87% Der p 23 (7.9 kU/L), 12% Der p 10 (0.02 kU/L) and 34% Lep d 2 (2.8 kU/L). Results showed no correlation between Der p 2 and Lep d 2 IgE levels (R=0.44), suggesting that these two molecules do not share enough epitopes to produce cross-sensitization.

Conclusion: Lepidoglyphus is an increasingly prevalent mite and should be included in the ITA due to lack of cross-reactivity with dust mites

Conflicts of interest: The authors did not specify any links of interest.

000870 | Single house dust mite allergens as potential biomarkers for allergic asthma and atopic dermatitis

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*Presenting author: T. Walsemann

Background: Despite 32 proteins from the European house dust mite (HDM) being officially registered as allergens today, the clinical relevance of many non-major allergens is not yet understood. And although component-resolved allergy diagnostics are strongly developing, only a fraction of HDM allergens are available for routine diagnostic platforms. This study therefore aimed to further elucidate the importance of several non-major HDM allergens and identify allergens associated with different allergic diseases such as asthma or atopic dermatitis.

Method: Sera from 384 HDM-allergic patients were analyzed in a serum-saving multiplex-assay with 9 different HDM allergens, namely Der p 1, 2, 5, 7, 10, 13, 20, 21, and 23, that were recombinantly produced in *E. coli.* Patients were divided into groups according to their phenotypes as obtained from medical history and standardized questionnaires. Statistical analysis was applied to identify allergens associated with clinical symptoms. The allergens Der p 5, 20 and 21 were subsequently integrated in the ImmunoCAP platform by streptavidin CAPs to quantify serum IgE concentrations in patients with different allergic phenotypes.

Results: Sensitization to more than three HDM allergens was associated with the simultaneous presence of multiple allergic diseases. Asthmatic adults were significantly more often sensitized against the lipophilic allergen Der p 21, and a similar trend was observed for Der p 5. However, the combined presence of sensitization to Der p 5 and Der p 21 did not lead to an increased asthma prevalence compared to individuals who were only sensitized against one of the two allergens. Atopic dermatitis patients were more often sensitized to Der p 5, Der p 20 and Der p 21 among others. Implementation of these allergens in the ImmunoCAP platform revealed that IgE concentrations against Der p 5 and 21 tended to be higher in patients with atopic dermatitis, but not in those with asthma without atopic dermatitis, compared to rhinitic-only patients. In particular, Der p 20-specific IgE concentrations above 80 kU/L were associated with severe atopic dermatitis in 75% of the patients and reached values up to 1500 kU/L.

Conclusion: This study demonstrates the clinical importance of the sensitization count and of certain allergens not available for routine

diagnostics yet, in particular Der p 5, 20, and 21. Implementing them as well as the sensitization count in diagnostic measures can improve diagnosis and risk assessment of HDM-allergic patients.

Conflicts of interest: LMR reports to have received project funding from Novartis Pharma GmbH outside of the submitted work.

001591 | Comparison of analytical performance of three multiallergen respiratory screening assays

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*Presenting author: P. Mathieu

Background: Multi-allergen respiratory screening tests aim to detect specific serum IgE antibodies to common airborne allergens. The methodological range has recently expanded, but the comparative performance of the available tests is not known.

Our objective was to evaluate the technical performance of three commonly used multi-allergen tests: SX01™ (Hycor®, Los Angeles, USA), Phadiatop™ (Thermo Fisher Scientific®, Uppsala, Sweden) and Alatop™ (Siemens® Healthcare GmbH, Erlangen, Germany).

Method: Retrospective analysis by SX01 and Alatop of 113 consecutive serum samples tested with Phadiatop™ (2019–2021, Synlab Provence, median age 18 years, range 2–78, sex ratio 1). Results were expressed as positive or negative according to the manufacturer's threshold (Phadiatop 0.35 kUA/L, SX01 0.17 kUA/L and Alatop index >0.9). The Phadiatop and Alatop tests comprise extracts of common airborne allergens (house dust mites, cat, dog, tree, grass and weed pollen, airborne moulds), as opposed to the SX01 test which is a mix of major and marker molecular allergens from house dust mites (Der p 1, Der p 2), cat (Fel d 1), dog (Can f 1, Can f 2, Can f 5), grass (Phl p 1) and tree (Bet v 1) pollen as well as the highly cross-reactive dog serum albumin Can f 3. Clinical data were collected for discordant cases.

Results: Positive results were found in 46% with Phadiatop, in 38% with SX01, and 40% with Alatop (Table). The interassay agreement for the 3 methods was 86% (97/113), i.e. 93% of negative results (57/61) and 75% of positive (39/52) results taking the Phadiatop results as a reference. Discordant results were predominantly positive with Phadiatop and negative with SX01 or Alatop, and associated with clinical history of allergic rhinitis. In two patients, isolated positive Alatop results were observed without a clinical history of allergic symptoms.

Conclusion: Despite differences in their composition, there was very good overall concordance of the three screening assays, remarkably for negative tests. The absence of fungal, insect, and some major grass allergens could explain the lower sensitivity of SX01 in our study. Conversely, biotin interference could be involved in isolated positive results with the Alatop mix

	Positive	Negative	TOTAL
Phadiatop	52	61	113
SX01	43	70	113
ALATOP	45	68	113
Concordance Phadiatop/SX01	81%	98%	90%
Concordance Phadiatop/Alatop	83%	97%	90%
Concordance SX01/Alatop	93%	94%	91%
Concordance Phadiatop/SX01/Alatop	75%	93%	86%

Conflicts of interest: The authors did not specify any links of interest.

000660 | Could specific IgE patterns to dog molecular allergens determine asthma risk?

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*Presenting author: S. S. Ozuygur Ermis

Background: Molecular allergology-based approaches are promising to provide a better risk assessment of allergic diseases and their outcomes. We examined the association between sensitization patterns to dog molecular allergens and asthma risk, and identified clinically relevant patterns in dog-sensitized adults.

Method: The study sample was from a population-based cohort, the West Sweden Asthma Study. Adults (16–75 years) were randomly invited to clinical assessment. Of 2006 subjects, those sensitized to dog dander extract ($n = 313$) were tested for positivity to dog molecular allergens (Can f 1-6). IgE levels ≥ 0.10 kUA/L were set as the cut-off for the positivity to dog molecular allergens. Single allergens were classified under two main groups: (i) dog-specific allergens (Can f 2/4/5) without any cross-reactivity or (ii) allergens with possible cross-reactivity (Can f 1/3/6) to cat allergens (Fel d 2/4/7). The presence of ever asthma was subdivided into (i) early childhood-onset (<7 years) (ii) late childhood-onset (7–19 years) (iii) adult-onset (≥20 years). Data were analysed using multivariate logistic regression models.

Results: Of dog-specific allergens, sensitization to Can f 4 was related to increased risk of current and ever asthma, but this was not the case for Can f 2 and Can f 5. In subjects with asthma, those

sensitized to Can f 2 and Can f 4 had a higher likelihood to have early childhood-onset asthma. Among cross-reactive allergens, Can f 3 and Can f 6 sensitization showed an increased risk of current and ever asthma. After stratification for cross-reactivity patterns, asthma risk was associated with cross-reactivity pattern to Can f 3 (Fel d 2[+]), but not with the primary sensitization to Can f 3 (Fel d 2[-]). Lastly, Can f 1 positivity was linked to having early childhood-onset asthma compared to other disease-onset patterns.

Conclusion: Subjects sensitized to Can f 1, Can f 2, Can f 4, and Can f 6 were more likely to have early childhood-onset asthma compared to late childhood- and adult-onset asthma. Cross-reactivity patterns of Can f 3 and Can f 6 were associated with the risk of ever/current asthma. Sensitization patterns to dog allergens might help to assess asthma risk.

	No. of positivity *n* (%)	Current asthma AOR (95% CI) [3] *n* = 221	Ever asthma AOR (95% CI) [3] *n* = 274	Ever asthma[3] Early childhood-onset AOR (95% CI) [3] *n* = 101	Ever asthma[3] Late childhood-onset AOR (95% CI) [3] *n* = 107	Ever asthma[3] Adult-onset AOR (95% CI) [3] *n* = 44
Sensitization to any dog-specific allergen (Can f 2/4/5)	200 (63.9)	1.17 (0.68-2.02)	1.30 (0.61-2.75)	1.23 (0.69-2.19)	0.90 (0.50-1.62)	0.86 (0.41-1.81)
Sensitization to Can f 2	71 (22.7)	1.87 (0.97-3.61)	1.67 (0.67-4.17)	**2.58 (1.38-4.84)**	0.65 (0.34-1.25)	**0.28 (0.09-0.86)**
Sensitization to Can f 4	105 (33.5)	**2.37 (1.31-4.28)**	**2.86 (1.16-7.04)**	**2.15 (1.23-3.77)**	0.66 (0.37-1.16)	0.52 (0.24-1.14)
Sensitization to Can f 5	162 (51.8)	0.97 (0.57-1.63)	1.16 (0.56-2.42)	1.15 (0.66-1.97)	0.89 (0.51-1.54)	1.01 (0.49-2.07)
Sensitization to any cross-reactive allergen (Can f 1/3/6)	212 (67.7)	1.69 (0.98-2.92)	**2.94 (1.41-6.15)**	**2.65 (1.36-5.15)**	0.75 (0.40-1.38)	**0.37 (0.17-0.78)**
Sensitization to Can f 1	167(53.4)	1.42 (0.85-2.38)	**2.11 (1.01-4.37)**	**2.52 (1.42-4.46)**	0.79 (0.46-1.38)	**0.31 (0.15-0.66)**
Can f 1 (+) Fel d 7 (-) Can f 1 (+) Fel d 7 (+) Missing data for Fel d 7	26 (8.3) 139 (44.4) 2(0.6)	1.08 (0.42-2.76) 1.42 (0.84-2.41) -	1.34 (0.29-6.19) 2.00 (0.93-4.29) -	1.77 (0.70-4.48) **1.95 (1.12-3.41)** -	0.64 (0.24-1.70) 0.91 (0.53-1.59) -	0.81 (0.22-3.05) **0.32 (0.15-0.70)** -
Sensitization to Can f 3	78 (24.9)	**3.07 (1.48-6.36)**	**3.06 (1.09-8.58)**	1.01 (0.53-1.93)	1.00 (0.52-1.93)	0.93 (0.41-2.15)
Can f 3 (+) Fel d 2 (-) Can f 3 (+) Fel d 2 (+) Missing data for Fel d 2	18 (5.8) 51 (16.3) 9 (2.9)	0.67 (0.24-1.89) **10.53 (2.93-37.81)** -	1.43 (0.30-6.81) **5.30 (1.11-25.28)** -	0.99 (0.31-3.12) 1.02 (0.48-2.17) -	0.61 (0.17-2.14) 1.40 (0.66-2.95) -	1.90 (0.53-6.80) 0.46 (0.14-1.46) -
Sensitization to Can f 6	122 (39.0)	**2.64 (1.48-4.69)**	**2.70 (1.15-6.34)**	**2.21 (1.27-3.86)**	0.64 (0.37-1.12)	0.55 (0.26-1.17)
Can f 6 (+) Fel d 4 (-) Can f 6 (+) Fel d 4 (+) Missing data for Fel d 4	8 (2.6) 106 (33.9) 8 (2.6)	N/A[4] **2.56 (1.39-4.72)** -	N/A[4] **3.06 (1.18-7.94)** -	1.49 (0.32-6.90) **2.02 (1.14-3.58)** -	1.13 (0.23-5.50) 0.64 (0.36-1.15) -	N/A[4] 0.67 (0.31-1.45) -
Polysensitization (≥3) to single dog allergen components	113(36.1)	**2.61 (1.44-4.72)**	**3.01 (1.24-7.30)**	**1.95 (1.11-3.43)**	0.66 (0.37-1.18)	0.66 (0.31-1.42)

[1]There were missing data for 22 subjects about information about age at asthma onset.
[2]Adjusted for gender, age, smoking status, body mass index, degree of urbanization, dust exposure at workplace, living on the farm during childhood, family history of allergy or asthma, and current ownership of a dog at home. Subjects without specific sensitization pattern were referent.
[3]Asthma phenotypes were analysed in the ever asthma subcategory. Subjects without specific sensitization pattern were referent.
[4]Inestimable due to small numbers

TABLE 1 Associations of sensitization to dog molecular allergens with risk of current asthma, ever asthma, and age at asthma onset: adjusted odds ratio (AOR) and 95% confidence intervals (95% CI).

Conflicts of interest: M.P. Borres is employed by Thermo Fisher Scientific (Uppsala, Sweden). B. Nwaru have received material from Thermo Fisher to perform the IgE analyses for this work. H. Kankaanranta reports fees for consultancies and lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma and SanofiGenzyme outside the current study. The rest of the authors declare that they have no relevant conflicts of interest related to this work.

001344 | Data mining in the world's largest set of over 280,000 real-life IgE-microarray measurements to answer open questions of molecular allergy diagnosis

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*Presenting author: C. Lupinek

Background: In molecular allergy diagnosis, many key questions to move the field forward are still unanswered due to lack of data. Examples of such research questions are the definition of surrogate markers for particular allergen (sub)families, country-specific sensitisation patterns, coverage of a particular allergen source by components, or species-specific IgE-reactivity of otherwise highly cross-reactive components.

Method: ALEX[2] (Macro Array Diagnostics, Vienna, Austria) is an IgE microarray comprising 178 allergen molecules and 117 extracts. To facilitate customer support and data-backup, all test results are saved on a GDPR compliant server. Until now, data from more than 280,000 measurements from 65 countries have accumulated. First descriptive statistics on those real-life data were generated with MS Power BI and Excel (Microsoft Corporation, Redmond, WA). Patients' data-privacy is warranted as only anonymised data were used.

Results: The following results are representative examples of different analyses performed so far. For nsLTPs, highly diverse reactivity patterns were observed, both for countries with high and low prevalences of LTP-sensitisation. Obviously, in this allergen family, both shared and a substantial number of species-specific epitopes exist, precluding the definition of surrogate markers for groups of LTPs.

Assessing coverage of weed extracts by components, this is accomplished for mugwort, where Art v 1 and 3 detected 94% of 25,000 cases, and ribwort (Pla l 1: 97% of 10,500), yet to a lesser extent for *Parietaria* (Par j 2: only 83% of 13,400) and ragweed (Amb a 1 and 4: 91% of 32,000).

IgE-reactivities to milk extracts from cow, goat, sheep, camel and mare revealed high agreement between goat, sheep and cow (75–84%, $n > 4400$), but much less with camel (30%). Mare's milk ($n = 1560$) seems to be allergologically distinct, since concordance with other species was consistently low (14–26%).

For *D. pteronyssinus*, considerable rates of monosensitisations to the marker allergens Der p 1, 2 and 23 were found (8%, 19% and 10% of 61,400). Despite similar sequence identities, Der p 2 and Der f 2 exhibited substantially stronger correlation than group 1 allergens (0.99 vs. 0.79), suggestive of identical epitopes for group 2 but discrepancies for group 1.

Conclusion: This largest set of IgE-microarray data represents a powerful resource to refine molecular allergy diagnosis and to monitor changes in global IgE-reactivity patterns over time.

Conflicts of interest: CL and PF are employees of MacroArray Diagnostics. AR is an employee of Adliance GmbH.

001090 | Influence of hazelnut varieties on Cor a 15 IgE-binding in hazelnut allergic pediatric patients

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Background: The lipophilic allergens, such as oleosins, are often poorly investigated and generally underrepresented in diagnostic tests. In addition to Cor a 12 and Cor a 13, the immunogenic power of the oleosin Cor a 15 was recently demonstrated for the hazelnut allergic pediatric patients. The aim of this work was: (i) to evaluate whether there are hazelnut varieties with reduced or increased Cor a 15 expression, (ii) to investigate whether the immunorecognition of Cor a 15 by hazelnut allergic subjects shows to be different according to hazelnut cultivars.
Method: Seventeen hazelnut cultivars, mainly from Italy, Turkey and Spain, were collected from an experimental hazel grove in Italy. A protocol optimized for the extraction of oil bodies associated proteins and the LDS-PAGE protein separation under reducing condition were performed. The pattern of specific IgE-binding of the oil body protein extracts was determined by immunoblotting, using a pool of sera from 20 pediatric subjects with a convincing history of hazelnut allergy. The tryptic digested proteins were identified by means of LC-MS/MS.
Results: The electrophoresis profile, confirmed by the LC-MS/MS protein identification, showed the presence of all the three allergenic oleosins Cor a 12, Cor a 13 and Cor a 15 in all the assessed hazelnut varieties. Cor a 15 resulted to be more expressed in Mortarella, Nocchione and Maraviglia varieties, conversely a reduced expression was observed in Tonda Gentile delle Langhe, Tonda di Giffoni and Bardina. The immunoblotting experiments showed the immunorecognition of Cor a 15 from all the tested varieties regardless of the oleosin abundance.
Conclusion: These results demonstrate that oleosins, especially Cor a 15, are highly conserved allergen between cultivars, highly recognized by Italian pediatric allergic subjects. Although, no significant differences in the immunoreactivity were found among hazelnut varieties, this analytical approach has a potential for the identification of varieties with reduced or variable allergen content.
Conflicts of interest: The authors did not specify any links of interest.

000625 | Youtube as a source of information for skin tests in the diagnosis of allergy

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Background: YouTube is increasingly being used for accessing information for both patients and physicians due to numerous medical videos, it contains. Although YouTube has advantages in this context, there are potential dangers since videos may contain nonscientific, misleading, or even harmful information. There are many videos about skin allergy testing used to diagnose allergic diseases, which are common health problems affecting both pediatric and adult population around the worldwide. Accurate diagnosis and optimal management of allergic diseases are very important for the health care systems. Therefore, we aimed to evaluate the popularity, usefulness and quality of YouTube videos regarding allergy skin tests.
Method: In this cross-sectional study, a search on YouTube was conducted using the term of "skin allergy tests". The most relevant 250 videos were initially screened. Videos in languages other than English, irrelevant (e.g., PPD skin test, heel prick test) ones, or videos with poor visual quality were excluded from the study. The remaining 133 videos were independently examined by two allergy specialists. Data on views, likes and comments as well as data on the source of uploaders, duration of availability and content quality were recorded. All videos were classified according to Global Quality Score (GQS)-(5-point score list) and Usefulness scoring systems (poor-moderate-excellent) to evaluate content quality (Image 1)
Results: Among the 133 videos, 82.7%, 14.3% and 3% of the videos were classified as scientifically correct, misleading, and potentially harmful respectively. 28.5% of the videos were non-procedural and general informative videos, while 71.4% of the videos were procedural demonstrative videos. 39.1% of the videos were posted on private individual's YouTube channels and TV shows whereas 60.9% were posted by healthcare providers, medical associations, hospital and clinics. The median of GQS scores of videos posted by healthcare workers were higher than the posted by non-healthcare workers ($p < 0.001$). The median of GQS score of non-procedural videos was lower than procedural videos ($p = 0.072$) (Image 1). Although the median views of videos posted by both healthcare and non-healthcare workers were similar, the median likes numbers of videos posted by healthcare workers were lower than the posted ones by non-healthcare ones ($p = 0.002$). Furthermore, videos uploaded by healthcare workers were more useful than the other ones ($p < 0.001$).
Conclusion: Our study demonstrated that the procedural YouTube videos on allergy skin tests posted by professional health care workers can be used as a source of information, while contents of some of the videos can be misleading or harmful. Therefore, professional medical organizations are needed to improve their visibility on YouTube so that the public can easily reach accurate information.

Assessment of video characteristics and Global Quality Scores (GQS) according to video type and channel source

Variable	Video type			Channel	Source	
	İnformative Videos(N = 38)	Procedural videos(N = 95)	P value	Healthcare Providers (MD, Medical ass., hospital and clinics) (N = 81)	Individual users channels/ TV shows (N = 52)	P value
Median of Views	3467 (41-1156441)	15007 (175-6925137)	0.002	9379 (41-6925137)	10648 (307-5222007)	0.202
Median of likes	33 (0-46000)	93 (0-31000)	0.005	45 (0-46000)	111 (1-27000)	0.002
Median of comments	3 (0-6400)	4 (0-3100)	0.439	2 (0-6400)	10 (0-3100)	<0.001
Median of video duration in minutes	4.77 (0.42-63.21)	4.07 (0.30-37.32)	0.443	3.41 (42-63.21)	7.14 (0.3-37.31	0.001
Median of Time Passed Since Upload (Days)	1320 (150-4500)	1500 (30-5190)	0.401	1470 (30-5010)	1350 (90-5190)	0.854
Median of View/Day	2.07 (0.03-1070.78)	8.49 (0.08-3108.34)	0.001	6.21 (0.03-1861)	5.7 (0.08-3108)	0.211
Median of Likes/Day	0.02 (0-42.59)	0.06 (0-27.78)	0.014	0.03 (0-42.6)	0.077 (0-27.8)	0.005
Median of Like/ View	0.8 (0-11.34)	0.57 (0-345.9)	0.369	0.5 (0-15.15)	0.81 (0.04-345.9	0.005
Global Quality Score	3 (1-5)	4 (1-5)	0.072	4 (2-5)	3 (1-5)	<0.001
Usefulness			0.399			<0.001
Poor	8(%6)	16(%12)		5(%4)	19(%14)	
Moderate	21(%16)	45(%34)		40(%30)	26(%19)	
Excellent	9(%7)	34(%25)		36(%27)	7(%5)	
Harmfulness			0.009			<0.001
Scientifically correct	26(%20)	84(%63)		77(%58)	33(%25)	
Misleading	11(%8)	8(%6)		3(%2)	16(%12)	
Potentially harmfull	1(%1)	3(%2)		1(%1)	3(%2)	

Median (Minimum-Maximum).

Conflicts of interest: The authors did not specify any links of interest.

000379 | Anomaly detection in pediatric lung function tests: A comparison of rule-based and machine learning methods

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*Presenting author: C. Martins

Background: Rule-based cut-offs are commonly used in clinical and epidemiologic settings to classify lung function tests as normal or not. These cut-offs are usually one-side based, which means that they only detect anomalies that deviate in one direction (upper or lower values than expected). We aim to test how unsupervised learning can be used to detect anomalies in pediatric lung function that are two-sided deviated and how different methods compare with each other.

Method: Spirometry and impulse oscillometry data before and after bronchodilation test was obtained from 1102 children aged between 14 and 15 years. A baseline model using rule-based criteria (FEV1 or FVC improvement >= 12% after bronchodilation, or FEV1 or FVC < 80% of predicted value, or R5 or R20 improvement >= 30% after bronchodilation, or R5 or R20 > 150% of predicted value) was established and used to calculate the approximate number of anomalies in the dataset. Machine learning (ML) models used were Support Vector Machines (SVM), Isolation Forest (IF), Principal Component Analysis (PCA), K-Means (KM) and Gaussian Mixture Models (GMM), and the Deep Learning (DL) models were Auto-encoders (AE), Deep Belief Networks (DBN) and Generative Adversarial Network (GAN). All models were fine-tuned to return between 15 and 20% of anomalies, according to the values obtained from the rule-based model. Cohen's kappa coefficient was used to classify the inter-model agreement.

Results: SVM and GAN showed the best inter-model agreement, with a substantial agreement with at least three other models. SVM and GMM were the best performers in unsupervised ML, returning 20% and 19% anomalies. The three DL models performed better when compared with classic ML models (except for SVM), returning 16% (AE), 17% (DBN) and 18% (GAN) anomalies. The agreement with baseline model was fair for SVM (0.28), GMM (0.28), AE (0.27) and GAN (0.24) models, however these results should be evaluated with caution since the baseline model only identifies results that anomaly deviate in one direction.

Conclusion: Different machine learning models showed consistency for anomaly detection in pediatric lung function with substantial inter-model reliability and can be used to assist physicians and researchers in detecting anomalies (disease cases or outliers).

BD	1								
SVM	0.28	1							
IF	0.15	0.30	1						
PCA	0.05	0.08	0.02	1					
KM	0.07	0.09	0.02	0.11	1				
GMM	0.28	0.66	0.31	0.06	0.08	1			
AE	0.27	0.66	0.37	0.07	0.07	0.56	1		
DBN	0.14	0.44	0.31	0.08	0.08	0.39	0.73	1	
GAN	0.24	0.76	0.42	0.06	0.06	0.66	0.72	0.49	1
	BD	SVM	IF	PCA	KM	GMM	AE	DBM	GAN

Cohen Kappa agreement for the different unsupervised learning models.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on pediatric allergy and prevention

100092 | Does maternal fermented dairy products consumption protect againts from cow's milk protein allergy in toddlers?

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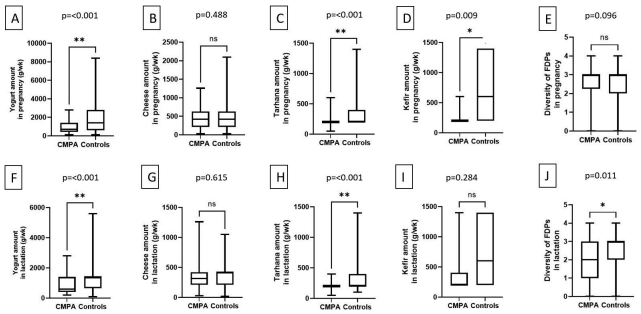
Background: Cow's milk protein allergy (CMPA) is the most common immunoglobulin E-mediated food allergy in childhood. To investigate the potential impact on the disease of the frequency, amount, and diversity of maternal consumption of fermented dairy products (FDP) during pregnancy and lactation in children with IgE-mediated CMPA.

Method: One hundred and sixty toddlers (80 with physician-diagnosed CMPA and 80 healthy controls) and their mothers participated in this case-control study. The data were collected using

a structured questionnaire and were compared between the two groups.

Results: The most commonly consumed FDP were cheese, yogurt, and tarhana. The amounts of maternal yogurt, tarhana, and kefir consumed during pregnancy ($p < 0.001$, $p < 0.001$, and $p = 0.041$, respectively) as well as yogurt and tarhana consumption during lactation ($p < 0.001$ and $p = 0.001$, respectively) were lower in toddlers with CMPA. The frequency of maternal consumption frequency of yogurt, cheese, and tarhana during lactation ($p = 0.001$, $p = 0.003$, and $p = 0.015$, respectively) and the diversity of FDP were also lower in toddlers with CMPA ($p = 0.001$). At multivariate logistic regression analysis, maternal weight gain during pregnancy (odds ratio [OR]:1.11, 95% CI:1.04–1.18, $p = 0.001$), maternal age (OR:1.20, 95% CI:1.09–1.31, $p < 0.001$), and gestational age at birth (OR:1.23, 95% CI:1.03–1.48, $p = 0.022$) increased the risk of CMPA, while the diversity of FDP consumed during lactation was protective against CMPA (OR:0.439, 95% CI:0.272–0.711, $p = 0.001$).

Conclusion: Weekly maternal consumption of FDP was low during pregnancy and lactation in toddlers with CMPA. While the diversity of FDP consumed during lactation may reduce the risk of CMPA, this effect was not observed during pregnancy.



Conflicts of interest: The authors did not specify any links of interest.

100096 | Determination of the effect of KIF3A gene polymophism in Turkish children with atopic dermatitis

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*Presenting author: H. Ercan Saricoban

Background: Atopic dermatitis (AD) is the most common chronic, pruritic, recurrent inflammatory skin disease in childhood. The literature has begun to reveal the relationship between the KIF3A gene (rs2897442) polymorphism and AD. To date, the relationship between atopic dermatitis and genetic mutation has not been demonstrated in Turkish population. It is aimed to investigate the KIF3A mutation and the inflammatory changes that occur in Turkish children with atopic dermatitis and their relationship with each other.

Method: The KIF3A gene (rs2897442) polymorphism was performed in 48 with atopic dermatitis and 46 healthy children aged 2 months to 16 years. Clinical data including age, gender, atopy status,SCORAD,presence of other concomitant allergic diseases,family history and eosinophil count, percentage, total Ig E, skin prick test results were recorded. DNA isolation and Real-Time PCR (RT-PCR) was then performed using the KIF3A detection kit. Statistical analyzes were made with SPSS 26.0 program.

Results: The KIF3A region of 48 patients with atopic dermatitis (M: 25, F: 23 with a mean age of 4.89 ± 3.67 years) and 46 healthy children in the control group (M: 27, F: 19 with a mean age of 3.76 ± 2.83) years was genotyped. Total IgE, absolute eosinophil count and eosinophil percentage are higher in individuals with atopic dermatitis than in healthy individuals. There was no significant difference between KIF3A genotype and atopic dermatitis and control groups ($p = 0.08$).Carrying the CC genotype increased the risk of atopic dermatitis disease 4 fold compared to the control group ($p = 0.043$, $\chi^2 = 4.610$, OR = 4.053, 95%). CI = 1.051–15.631). Carrying the T allele protects against atopic dermatitis ($p = 0.040$, OR = 0.235, 95%. CI = 0.061–0.905). TT genotype had lower absolute eosinophil counts ($p = 0.023$), and those with C allele had higher values ($p = 0.023$). No statistically significant relationship was found between the KIF3A gene polymorphism and the severity of atopic dermatitis.

Conclusion: It is the first pilot study showing the risk of KIF3A gene polymorphism in the development of atopic dermatitis for the Turkish population. Carrying a homozygous C (CCgenotype) increases the risk of developing AD,and carrying the T allele decreases the risk of AD. TT genotype had lower absolute eosinophil counts, and those with C allele had higher values.

Conflicts of interest: The authors did not specify any links of interest.

100182 | Retrospective review of the pollen subcutaneous immunotherapy service at Sheffield Children's Hospital

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*Presenting author: W. S. W. Fong

Background: Subcutaneous immunotherapy (SCIT) is an effective treatment for severe pollen induced allergic rhinoconjunctivitis (AR). The SCIT service at Sheffield Children's Hospital (SCH) was established in 2014 and patient numbers have grown significantly since.

Method: The medical records of all patients who received pollen SCIT between 2014 and 2022 were reviewed, to evaluate:

1. Demographic and clinical patient characteristics
2. Adherence to guidelines in terms of patient selection
3. Referral sources
4. SCIT-related adverse events (AEs) and their impact
5. Treatment outcomes (patient-reported disease severity scores, quality of life impact and medication use).

Relevant patient data was collected and anonymised.

Results: 62 children and young people (66% male), were initiated on pollen SCIT (mean age at initiation 14 years). 56% had at least one other atopic comorbidity, most commonly asthma (33%). 40% were referred from primary care, 26% from within SCH, and 34% from other secondary care centres. AR was suboptimally treated at referral in 48% of patients. The mean time from referral to SCIT initiation was 1.5 years (range: 0–5 years). Patients reported severe symptoms requiring oral steroid use ($n = 11$) and negative disease impact on school performance ($n = 51$), sleep ($n = 38$), and outdoor activities ($n = 41$). The average VAS score pre-SCIT was 3.38 out of 5.

98% and 61% received Pollinex Quattro Grass and Pollinex Quattro Tree respectively, with 60% receiving both.

Forty patients experienced mild AEs, most commonly delayed local reactions ($n = 23$). None led to SCIT discontinuation, except a single patient who had anaphylaxis (treated with one dose of im Adrenaline) and was converted to sublingual immunotherapy.

Five patients (8%) discontinued SCIT due to pregnancy during COVID pandemic (1), IBD flare (2), missed appointments (1) and asthma deterioration (1). Twenty-three patients are due their 2nd or 3rd SCIT cycle. Thirty-four patients completed 3 years of SCIT, with 97% of those reporting symptom improvement (VAS score 2.1) and 73% reporting reduction in AR medication use.

Conclusion: The pollen SCIT service in SCH has expanded successfully, with equitable access, high adherence to patient selection guidelines, low drop out rates, safe administration and highly favourable treatment outcomes.

Conflicts of interest: The authors did not specify any links of interest.

100195 | Iron deficiency anemia in children with atopic dermatitis and risk factors

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Background: Allergic food avoidance, chronic inflammation, and immunosuppressive drug use are associated with anemia in atopic dermatitis. In this study, we aimed to investigate not only the frequency of iron deficiency anemia in children with atopic dermatitis by comparing them to healthy children but also the comorbid risk factors affecting this frequency.

Method: Medical records of 100 children aged 0–6 years with atopic dermatitis (case group) and 100 healthy children in the same age group without atopic dermatitis (control group), who applied to Sivas Numune Public Hospital from May 2019 to October 2019, were analyzed retrospectively.

Results: In our study, the frequency of microcytic anemia with iron deficiency was found to be higher in children with atopic dermatitis (15%) than in healthy children (5%) ($p < 0.001$). Increased scorad severity ($p = 0.013$), early onset (< 2 years) ($p = 0.024$), skin infection (p-value = 0.013), breastfeeding more than 6 months ($p = 0.036$), asthma (p-value = 0.013), food allergy (p-value = 0.013), particularly multiple food allergies ($p < 0.001$) were associated with a higher frequency of iron deficiency anemia in children with atopic dermatitis. Hay fever, family history of atopy, large family size, and the socioeconomic level of parents were not significantly linked to a higher frequency of iron deficiency anemia in children with atopic dermatitis.

Conclusion: Iron deficiency anemia was significantly more common in children with atopic dermatitis than in healthy children, especially when food allergies, asthma, skin infection, breastfeeding for more than 6 months, and severe scorad score were present. There is a need for more comprehensive studies to investigate this relationship and its affecting factors in the future.

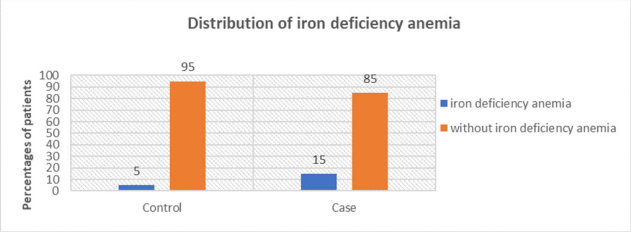

FIGURE 1 Distribution of iron deficiency anemia in contol and case group.

	AD with İDA (n:15, 100%)	AD without İDA (n:85, 100%)	P value
Female, n(%)53	8 (53.3)	45 (52.9)	0.384
Age of AD onset, median, month (25-75 percentil)	12 (2-41)	39.5 (13.7-72)	**< 0.001**
Early onset of AD (<2 years)	12 (80.0)	40 (47.4)	**0.024**
Low Economic level (household income)	8 (53.3)	48 (57.6)	0.392
Education level	8 (53.3)	47 (55.3)	0.495
Large family size	5 (33.3%)	33 (38.8%)	0.358
History of atopy	12 (80.0)	43 (50.6)	**0.028**
Family history of atopy	7 (46.6)	42 (49.4)	0.457
Consanguinity	6 (40.0)	28 (32.9)	0.212
Severe AD	12 (80.0)	30 (35.3)	**<0.001**
Skin infection	10 (66.6)	21 (24.7)	**<0.001**
Breastfeeding > 6 months	12 (80.0)	48 (57.6)	**0.036**

TABLE 1 The risk factors associated with iron deficiency anemia in the patients with atopic dermatitis

Conflicts of interest: The authors did not specify any links of interest.

100280 | Identification of metabolic biomarkers associated to allergic diseases in newborns

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Background: Allergic inflammatory diseases have experienced a constant increase in prevalence and severity in recent decades. It is necessary to understand the underlying causes of this increase and identify new biomarkers to improve diagnosis and decide the best intervention strategies. The general objective of this project is to find, by -omics techniques, metabolic biomarkers in newborns that allow to predict the development of inflammatory pathologies associated with the most prevalent allergies in the first years of life (i.e., atopic dermatitis; allergic asthma and/or food allergy).

Method: Newborn serum samples are collected at 48h of life during the neonatal endocrine metabolic screening (neonatal heel prick test). Those subjects who during the recruitment phase (18 months) are diagnosed with any of the above-mentioned allergies will be included in the case group, and those who don't will be the control group. In this study, 40 serum samples, undefined as control or case yet, were subjected to the Olink$_{TM}$ Target 48 Cytokine panel analysis (ref. 93200 Olink®, Uppsala). This proteomic approach allows the simultaneous analysis of 45 protein biomarkers related to cytokine signaling and inflammatory processes.

Results: Protein concentration of inflammation-related human protein biomarkers was measured by a Proximity Extension Assay (PEA). Data analysis was performed by employing a pre-processing normalization procedure. Absolute quantification made through a precise pre-defined standard curve for each protein showed a different range of proteins concentration among serum samples. Some of the highly expressed cytokines were mediators of allergic inflammation, such as IL-4, IL-6, IL-13, IL-33 and TSLP. These cytokines may be potential players in the pathogenesis of inflammatory allergic diseases. Inflammation causes weakening of epithelial barriers at the mucosal level, increasing their permeability and therefore allergen sensitization is prone to occur. Follow-up of these patients will be necessary to confirm whether or not they develop any inflammatory allergic disease later in life.

Conclusion: At present, there are no specific serum biomarkers that can be used in the prediction and evolution of allergic pathology. The results from this study will be integrated with the results obtained from other omics platforms. These data together with the clinical follow-up, will provide a set of predictive metabolic biomarkers of inflammatory pathologies associated with allergy early in life. In addition, our group has previously identified a panel of 29 metabolites that could be considered potential biomarkers associated with the evolution to severity in allergic pathology. In future studies

we intend to validate the metabolites observed with this panel of severity biomarkers that we already have.

Conflicts of interest: The authors did not specify any links of interest.

100403 | Establishment and promotion of the "Five-in-One" strategy for precise allergic disease prevention and control

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Background: Establishment and Promotion of the "Five-in-One" Strategy for Precise Allergic Disease Prevention and Control.

Method: Implement the "Five-in-One" strategy (pollen monitoring, vegetation research, epidemiological investigation, general practitioners and specialists training, and health education for the public) for precise allergic disease prevention and control.

Results: Pollen monitoring explicited the types, quantities, and seasonal changes and diffusion pattern of the most common pollen in various regions;Vegetation research demonstrated the distribution pattern and characteristics of the most common pollen in multiple areas; Epidemiological investigation illustrated the prevalence and significant risk factors of allergic diseases; General practitioners and specialists training enhanced the comprehensive diagnosis and treatment capabilities of doctors, and standardized the diagnosis and treatment of allergic diseases;Health education for the publicimproved the public's awareness of allergic diseases. The "Five-in-One" precise allergic disease prevention and control strategy was extensively advocatedand implemented in Beijing, Inner Mongolia, Xinjiang, and Hebei province in China, and made incredible achievements. In these regions, hierarchical diagnosis and treatment were implemented, a green channel for referral system was developed, and access to health care were more equitable.

Conclusion: The "Five-in-One" strategy for precise allergic disease prevention and control has created a new model for treating allergic diseases in China, which were acknowledged by local governments and peers. Numerous governments have identified the strategy as one of the most critical initiativesfor people's livelihoods. The strategy shifts medical care from treatment to prevention, maximizes the role of the Association of Allergology, disseminates high-quality medical resources of the allergology to primary level, resolves the issue of locals seeking medical treatment, and promotes the development of allergology in northern China.

Conflicts of interest: The authors did not specify any links of interest.

100487 | Why molecular diagnostics is important to have a personalized treatment plan of cow's milk allergy in children?

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Background: Cow's milk protein allergy is an urgent problem in pediatrics and affects from 0.5% to 3% of infants under one year. IgE-dependent form is present in 60% of children with cow's milk protein allergy and occurrence of symptoms is usually observed from several minutes to several hours from the time of allergen consumption. Molecular diagnostics opens many new opportunities for diagnosing different forms of allergy and prognosticating efficacy of treatment.

Method: Inclusion criteria of the investigation: children from six month to three years old, positive skin test to milk (papule ≥3 mm with prick method) and specific IgE to milk ≥0.35 kUa/L, positive oral provocation test. Assessment of a molecular profile was performed for detecting major components of milk (Bos d 8, Bos d 5, Bos d 4), minor (Bos d 6) and cross-reactive ones with serum albumin (Fel d 2, Can f 3).

Results: Molecular allergy diagnostics with the determination of IgE specific to components of milk allergens and cross-reactive albumins (ALEX, MacroArrayDX, Austria), namely to Bos d 8, Bos d 5, Bos d 4, Bos d 6, Fel d 2 and Can f 3, was carried out for the in-depth study of indications for SOTI and prediction of its effectiveness in children of the study group, within the grant program at the Department of Pathophysiology and Allergy Research of the Vienna Medical University (Vienna, Austria).

Evaluation of the molecular profile showed that the highest rates were in the group of three major molecules: casein (Bos d 8), β-lactoglobulin (Bos d 5), and α-lactalbumin (Bos d 4). The Pearson and Spearman correlation coefficients allowed us to study statistically significant correlations between the two corresponding signs. It was found that casein (Bos d 8), as the major component of milk, has a statistically significant correlation with the diameter of the papule ($r = 0.44$), Can f 3 ($r = 0.39$), and Bos d 4 ($r = 0.28$). Bovine serum albumin (Bos d 6) has a statistically significant correlation with Fel d 2 ($r = 0.64$) and Can f 3 ($r = 0.44$), indicating cross-reactivity with animals, including cats and dogs. It has been proven that independent predictors, which reduce the likelihood of tolerance development in the elimination diet, are papule diameter over 5 mm and Bos d 8, Bos d 5, Bos d 4, Bos d 6 at a concentration of ≥0.35 kUa/L. The low likelihood of tolerance development by elimination therapy (less than 50 %) is a recommendation for prescribing treatment by specific oral tolerance induction.

Conclusion: Assessment of a molecular profile is important for diagnosis and treatment of cow's milk protein allergy irrespective of a choice of therapeutic tactics – specific oral tolerance induction or elimination diet.

Conflicts of interest: The authors did not specify any links of interest.

100497 | Raising allergy and immunology awareness by means of social media platforms

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Background: One of the main challenges in the field of allergy and immunology is the adherence and dropout of patients from treatments (ex. Asthma/immunotherapy). This might be due to a lack of disease awareness. One of the factors contributing to this issue is the limited time and technical medical language used during patient-physician consultations. One of the main ways to ensure the divulgation of medical information is via social media through the creation of visual, written or audio content (Facebook, Instagram, Twitter). Even though these platforms represent a useful tool, they present some pitfalls. As an example, it has been previously demonstrated that False news on Twitter diffuse faster than true news. The objective of this study is to evaluate the diffusion and engagement of Allergy and Immunology-based video and audio content on social media.

Method: We created 4 short podcasts and video episodes (duration time between 3–4 min) on allergy and immunology topics. The podcasts were edited using audio editing software, FL Studio, and uploaded to the Spotify platform. The videos were recorded and edited using Adobe Premiere Pro. For both podcast and videos we used professional microphone (Rode Nt1). Both podcast and videos were promoted on social media platforms, Instagram, Facebook and Twitter. Thus, we have calculated the absolute number of reached accounts (followers vs non followers; engagement metrics).

Results: the analysis of the absolute numbers of engagement metrics demonstrated that video content obtained a higher interaction rate compared to audio content. Moreover, the audio content is able to reach more not follower accounts than the audio content suggesting that creating video content represents a more effective strategy for increasing awareness among the target audience. In support of our study, we provide the analyzed data for the four episodes, including the number of accounts reached among both followers and non-followers.

Conclusion: Our study demonstrate that the social media platforms are a useful tool for divulgation of Medical information in Allergy and Immunology field. According to our data the video content represents a more effective strategy for increasing awareness among the target audience. One of the possible explanations might be that the video contents maybe more user-friendly. (More dynamic and immersive experience for the viewer)

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on food allergy

100019 | A retrospective comparison of IgE-mediated cows milk protein allergy management

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*Presenting author: J. Trujillo

Background: Cow's milk protein allergy (CMPA) is one of the most common food allergies in infancy and childhood, affecting approximately 1% of Irish infants and between 0.3 and 7.5% of infants in Spain. The management of Cow's Milk Protein Allergy (CMPA) is debated around the world.

Complete avoidance of milk protein is still the usual treatment in several countries. The baking process alters the structure of different milk allergens' changing its stability and subsequently creating a decreased allergenicity, and a baked milk ladder has been used in Ireland as a method of reintroduction of milk in IgE-mediated CMPA. EAACI recommends oral immunotherapy (OIT) for CMPA in children around 4–5 years of age in order to increase the threshold of reaction while on treatment in children with persistent CMPA.

This study aims to evaluate the use of three different strategies for treating IgE-mediated CMPA by comparing the rate of acquired tolerance of three cohorts of paediatric patients diagnosed with CMPA from the three hospitals participating in this study.

Method: This is a retrospective chart review of 600 paediatric patients from the population who have been treated for IgE-mediated CMPA between 2011 and 2020; with the milk ladder in Ireland; early reintroduction of pasteurized milk in Spain and with complete avoidance followed by an oral food challenge in Spain.

The main outcome was the introduction of cow's milk proteins. Secondary outcomes included skin prick test wheal size and milk specific IgE at diagnosis, history of other atopic conditions and allergic symptoms experienced during the treatment.

Results: Successful treatment was achieved in 462 (80.9% of the patients of the whole sample. The proportion of success in the milk ladder group was 86.6% (95% confidence interval (CI): 80.6–90.9), lower than the obtained in the early gradual milk introduction group (96.0%; 95% CI: 92.3–98.0). Both strategies had a significantly higher success rate than milk avoidance (61.0%; 95% CI: 54.1–67.5)

There were significant differences between the three cohorts regarding accidental exposure to milk. Milk avoidance was the least safe treatment, with 106 patients experiencing an accidental exposure to milk, 34 of these resulting in an anaphylactic reaction. Although milk ladder had more patients with an exposure than early

introduction (18.7% vs. 0.5%; $p < 0.01$), there were no differences in the proportion of anaphylactic episodes.

In the milk avoidance group a higher value of the Skin Prick Test was associated with a failure in the treatment ($p < 0.01$). That difference wasn't found in the other two groups. In the milk ladder group, a higher value of whole milk specific IgE was associated to a failure of the treatments. This was also seen in the milk avoidance group.

Conclusion: Cow's milk can be successfully and safely reintroduced using different treatment strategies other than strict avoidance. This is the first study that compares outcomes of patients undergoing these 3 different strategies for CMPA management, providing a foundation for the creation of new projects that will help to develop new ideas for the management of CMPA.

Conflicts of interest: The authors did not specify any links of interest.

100159 | Remodeling and infiltration of effector cells in the oral mucosa of patients with severe allergy to LTPs

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Background: Lipid transporter proteins (LTPs) are the most frequent cause of food allergy in adults in the Mediterranean area. LTPs are low molecular weight proteins resistant to degradation, which increases their sensitization capacity and thus the severity of symptoms. This causes people to have a poor quality of life, with a higher probability of suffering digestive problems or anaphylactic shock. Recently, it has been shown that patients with severe respiratory and food allergies induced by profilin and mites have a dysfunction in the integrity of the epithelial barrier of the oral mucosa, which facilitates the penetration of allergens and the generation of a local inflammatory response. Nonetheless, it is not known if this could be the problem of patients with LTP allergy as there are no studies on the integrity of their oral epithelial barrier and its associated mucosal immune system.

The aim of the present study was to evaluate the association between severe allergic phenotypes in allergy to LTPs and oral mucosa barrier defects. As the inflammation that develops in these patients is possibly related to epithelial barrier loss and remodelling, the oral mucosa was used as an accessible and safe tissue for patients to investigate what happens in the mucosa during a severe allergic response.

Method: Twelve patients allergic to LTPs were stratified according to clinical manifestations, severity by Muller classification and IgE recognition patterns into grades I and II ($n = 6$) and III ($n = 6$), as well as six control subjects. Oral mucosal biopsies were taken for histological sections and subsequent immunohistochemical staining and counting of cells positive for different markers such as CD19, MCT, CD3, CD4 and elastin, and staining and measurement of claudin-1, occludin and E-cadherin levels.

Results: Preliminary results indicate that patients classified in group III show a decrease in the number of cell junctions, suggesting a higher degree of remodelling. In addition, these patients show an increased recruitment of CD19 cells in the oral mucosa. Surprisingly, patients with allergy to LTPs had lower numbers of MCT cells compared to control patients.

Conclusion: Severely allergic patients to LTPs show significant damage in the oral mucosal epithelial barrier, which favors local inflammation and increased recruitment of effector cells.

Conflicts of interest: The authors did not specify any links of interest.

100239 | Qualitative study on parents' perspectives on the prediction and prevention of food allergy in children (NAMIBIO-App)

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Background: The last decade has seen a paradigm shift towards allergy prevention. Parents have to deal with large amounts and, in some cases, changing information and new evidence that often contradicts previous assumptions.

Our study is part of the NAMIBIO-App consortium, which aims to develop an app to predict food allergy in children and guide parents of children at high risk towards prevention and timely tolerance induction. We aimed to explore and understand parents' perspectives on information seeking behaviour, information needs as well as requirements for an app to predict and prevent food allergy in children.

Method: We used a qualitative approach with topic-guided interviews with parents of children (0–3 years) diagnosed with food allergy, at risk of or without a known risk of food allergy. We analysed the data according to Kuckartz's qualitative content analysis and formed four main categories with inductive subcategories.

Results: We conducted 30 interviews (one in person, 11 by phone, 18 online) with parents: 26 mothers, three fathers and one couple. Parents sought information for emotional or rational reasons and expressed a need for more competence in seeking information. Some did not express any information needs, while others voiced a need for information on preventive measures. Healthcare providers, health education/patient organizations, digital and print media and informal exchange were named as sources of information for food allergy prevention and prediction. In terms of app requirements parents wished for an app provided by experts that is non-commercial/free of charge where minimal data is used in a safe way.

Conclusion: There was a diversity in expressed need and competence regarding food allergy prevention and prediction. Not all parents wished for information on allergy prevention, but those who did were rather clear about requirements for a digital application on food allergy prevention and prediction. They had low concerns about providing personal data in an app and were open for using digital support for the prevention of food allergies in children.
We conclude that raising awareness on food allergy prevention and prediction as well as helping parents becoming allergy prevention literate appears to be important. The planned NAMIBIO app may be a promising tool to help achieve this.
Conflicts of interest: The authors did not specify any links of interest.

100407 | Citrin: A novel food allergen in citrus seeds and citrus-derived pectin that shows cross-reactivity with cashew and pistachio

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Background: Patients exquisitely sensitive to cashew/pistachio are at risk for allergic reactions to citrus seeds and pectin. In this study, we sought to examine whether pectin is contaminated with citrus seeds, to identify a culprit antigen in citrus seeds, and to assess for cross-reactivity among allergens in citrus seeds, citrus pectin, and cashew/pistachio.
Method: Proteins from orange seed coats, orange seed endosperms, lemon seeds, grapefruit seeds, apple seeds, citrus pectin, apple pectin, and grapefruit pectin were extracted. Protein concentrations in all extracts were determined and visualized using SDS-PAGE gels. IgE binding capacity was determined with Western blot analyses and Tandem Mass spectrometry (MS/MS) for the identification of the culprit allergen in citrus seeds and pectin.
Results: In subjects with citrus seed, pectin, and cashew allergies, there was strong IgE-reactivity to bands between 17–28 kDa and 28–38 kDa. The MS/MS analysis of these bands indicated the presence of citrin as the culprit allergen. Citrin and Ana o 2 are both 11S globulins belonging to the cupin superfamily, and significant homology was demonstrated between these proteins.
Conclusion: Citrus pectin may be contaminated with citrus seeds. Citrin, a newly identified allergen in citrus seeds, appears to be the culprit antigen in citrus seeds and contaminated citrus pectin. Citrin is highly homologous with Ana o 2 in cashew and Pis v 2 in pistachio, suggesting potential for cross-reactivity and providing an explanation for co-allergenicity of cashew/pistachio, citrus seeds, and citrus pectin.
Conflicts of interest: GNK: George N. Konstantinou is or recently was a speaker and/or advisor for and/or has received research funding from AstraZeneca, Chiesi, GSK, Menarini, Novartis, Nutricia, Pfizer, Sanofi, and Vianex; he serves as the secretary of the Food Allergy Interest Group of the EAACI, and as a member of the Medical Advisory Board of the International FPIES Association MGB: Mary Grace Baker receives research support from the Louis and Rachel Rudin Foundation, NIH/NIAID, Pfizer, and DBV Technologies. HA: Hugh Sampson receives funding to his institution for grants from the National Institutes of Health/National Institute of Allergy and Infectious Diseases and is employed part-time by and has received stock options from DBV Technologies. He reports consultancy fees from N-Fold, LLC, DBV Technologies, and Siolta Therapeutics, as well as royalties from Elsevier. SHS: Scott Sicherer reports royalty payments from UpToDate and from Johns Hopkins University Press; grants to his institution from the National Institute of Allergy and Infectious Diseases, from Food Allergy Research and Education, and from Pfizer, Inc.; and personal fees from the American Academy of Allergy, Asthma and Immunology as Deputy Editor of the Journal of Allergy and Clinical Immunology: In Practice, outside of the submitted work. ANW: Anna Nowak-Wegrzyn receives research support from Alladapt Immunotherapeutics, DBV Technologies, Siolta Therapeutics, and Regeneron; speaking fees from Nestle, Danone, and Thermofisher; royalties from UpToDate; she serves as an Associate Editor for the Annals of Allergy, Asthma and Immunology, Director of the AAAAI Board, and the Chair of the Medical Advisory Board of the International FPIES Association.

100481 | Omalizumab for severe food allergy in a large Italian cohort of asthmatic children

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Background: No current recommendation includes omalizumab (anti-IgE) for the treatment of food allergy (FA). The effects of omalizumab as monotherapy in FA thresholds and adverse reactions in the event of accidental ingestion are not well-known.
Objective: We assessed the impact of omalizumab in terms of efficacy, safety, and quality of life (QOL) in patients with moderate/severe asthma and FA in a single-center, longitudinal, open label study.
Method: Since August 2014 we have been consecutively enrolling in our Italian research pediatric hospital all children (6–18 years) eligible for omalizumab because of severe asthma with concomitant food allergy.

Each patient underwent diagnostic oral food challenges (OFC) before (T0) and at least 4 months after (T1) the first omalizumab administration in order to establish the threshold of reactivity to the culprit food(s). Those who did not pass the second OFC at T1 underwent a third and a fourth OFC at least 8–12 months after first omalizumab administration (T2-T3).

Omalizumab was administered every 2 or 4 weeks, according to the patients' weight and IgE level, as per the asthma indication.

Results: At 4–6 months of omalizumab therapy (T1), 97/153 (63.4%) were fully tolerant the specific food allergen. At T2 the last dose was tolerated in 20/56 (35.7%), and at T3 the last dose was tolerated in 2/36 (5.6%). Over time 119/153 patients (77.7%) passed OFC. An increase in the threshold of reactivity was reported overall in 90% of patients/food.

Omalizumab dosage per weight alone was strongly associated with an increase in the threshold ($p < 0.0001$).

Conclusion: Omalizumab resulted as a promising, effective, and safe treatment option in food allergy able to induce an increase in the threshold of food reactivity and consequently, an achievement of the ad libitum diet. Further studies are needed to confirm our data.

Conflicts of interest: Outside this work Stefania Arasi and Alessandro Fiocchi received feed for occasional advisory board (Novartis). This has no influence on this work.

Flash talks on atopic dermatitis

000616 | Longitudinal evaluation of the skin barrier using new non-invasive portable electrical impedance device: A birth cohort study in infants at high risk of atopic dermatitis

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Background: We developed a non-invasive portable electrical impedance device (Skin Barrier Meter) to measure the estimated transepidermal water loss (e-TEWL), the water content of the skin stratum corneum, and the thickness of the skin stratum corneum. Skin Barrier Meter (SBM) can measure all of them with a simple technique in 5 seconds. We aimed to evaluate the skin barrier in infants at high risk of atopic dermatitis (AD) longitudinally with SBM.

Method: This study was a prospective birth cohort, recruited newborns whose parents or siblings had history of atopic dermatitis within six days of birth at the National Center for Child Health and Development, Japan. Preterm births and newborns with skin diseases or severe complications were excluded. We measured e-TEWL, the water content and the thickness of the skin stratum corneum in the foreheads, cheeks, forearms, and calves with SBM periodically until 9 months of age.

Results: Thirty newborns from January to July 2022 were included for analysis. The median age at first measurement was four days old (range 2–6 days), and 13 (43.3%) were boys. Twenty (66.7%) infants developed atopic dermatitis at 4 months old (median, range 2–6). The skin barrier changed rapidly during the neonatal period. In all infants, the water content of the skin stratum corneum and e-TEWL increased and the thickness of the skin stratum corneum decreased. The AD infants showed a significant decrease in the thickness of the stratum corneum in the foreheads during the neonatal period, compared to the non-AD group ($p = 0.03$). There were no adverse events caused by the SBM.

Conclusion: The significantly decreased thickness of the stratum corneum during the neonatal period was associated with the development of atopic dermatitis in infancy. The SBM is a novel non-invasive, portable electrical impedance device which could measure the skin barrier in infants from neonatal period safely.

Conflicts of interest: Osamu Uehara, Yuya Funaki and Kentaro Narumi are employees of ALCARE Co. Ltd., Tokyo, Japan.

000482 | Dupilumab-induced conjunctivitis in atopic dermatitis patients is not associated to a decreased expression of conjunctival tight junctions

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*Presenting author: C. Rondon

Background: Dupilumab (DU) is effective in atopic dermatitis (AD) and T2 asthma (AS) patients, but is associated to ocular surface alterations in the former subjects only. This side effect might be associated to the impairment of the conjunctival barrier. In this study, we investigate the clinical and histopathological features of DU-associated conjunctivitis.

Method: 20 patients with severe AD on DU (AD-10), 10 patients with severe AD on cyclosporine (AD-CY), 10 patients with mild-to-moderate AD on topical therapy (AD-TOP), and 10 patients with severe T2 asthma on DU and no associated dermatosis (AS-DU) were recruited (treatment duration >3 months). Baseline AD severity was scored according to EASI, and OSDI was measured on treatment in all individuals. All subjects underwent ophthalmological examination before being collected an impression cytology of the ocular surface (unilateral), which was used to investigate the expression status of tight junction and mucin genes by qPCR.

Results: EASI was higher in both AD-DU and AD-CY, as compared to AD-TOP and AS-DU groups ($p < 0.001$ in all cases), whereas no difference was observed between AD-DU and AD-CY individuals. OSDI was normal in all subjects in the AD-CY, AD-TOP and AS-DU

groups, whereas 10% of AD-DU subjects showed mild-to-severe affection. Conjunctival scarring, blepharitis, and keratitis were significantly more frequent ($p < 0.01$ for all comparisons) in AD-DU patients than in subjects from the other groups, whereas no significant differences were observed between AD-DU individuals and patients from any other group regarding palpebral inflammation, papillary/follicular reaction, and ocular secretion and hyperemia. No significant differences were observed in the mRNA expression of *claudin-1*, *claudin-4*, *claudin-7*, *occludin* and *ZO-1* among the different groups. Conversely, the expression of mucin gene *MUC5AC* was s higher in AD-TOP patients as compared to subjects in the AD-CY and DU-AS groups ($p < 0.01$ in both cases). A similar trend was seen between AD-TOP and AD-DU individuals, although the differences were not significant.

Conclusion: Severe T2 inflammation in epithelial barriers (either skin or bronchial mucosa) is associated to a decreased expression of conjunctival mucins. DU-treated AD patients exhibit greater symptoms and alterations in the ocular surface than severity-matched AD individuals or subjects receiving DU for other indication. Nevertheless, DU-induced conjunctivitis in AD patients is not related to a decreased expression of conjunctival tight junctions.

Conflicts of interest: The authors did not specify any links of interest.

000385 | Baseline demographics, comorbidities and disease burden in patients with atopic dermatitis: An update from the GLOBOSTAD observational study

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Background: The efficacy and safety of dupilumab has been reported previously based on data from controlled clinical trials. The GLOBOSTAD study adds to the existing body of evidence by providing data from a real-world setting. This analysis reports baseline demographics, comorbidities, and disease burden in patients with atopic dermatitis (AD) who received treatment with dupilumab in a real-world setting.

Method: This 5-year, international, multicenter, noninterventional observational study (GLOBOSTAD; NCT03992417) included patients ≥12 years old with AD who initiated dupilumab treatment based on country-specific prescribing information. Data reported are for the population at baseline ($N = 952$, data cutoff: March 2022).

Results: In the 952 patients included at baseline, mean (standard deviation) age was 35.5 (13.6) years. 57.8% of patients were male and 65.2% were White. 77.8% of patients reported type 2 inflammatory comorbidities, including allergic rhinitis (51.7%), asthma (33.9%), food allergies (30.9%), allergic conjunctivitis (17.9%), and other allergies (28.8%). 10.9% had reported visiting the emergency room or an urgent care center for their eczema. The main reasons for doing so reported in the Health Care Resource Utilization Questionnaire (HCRU) were eczema flare (49.2%), unbearable itch (27.0%), and skin infection (19.0%). At study entry, 69.3% of adult patients were employed. Based on the Work Productivity and Activity Impairment Questionnaire for AD (WPAI-AD), which assesses the hours worked and missed due to health, as well as the degree to which health affected productivity during work and other activities, patients reported a 46.9% overall work impairment and a 48.0% activity impairment due to their health.

Conclusion: In a large majority of GLOBOSTAD patients, AD was associated with type 2 inflammatory comorbidities and represented a considerable burden impacting their work and other activities.

Conflicts of interest: Ardeleanu M: Regeneron Pharmaceuticals, Inc. – employee and shareholder. Wu J, Bosman K: Sanofi – employees, may hold stock and/or stock options in the company. Chu CY: AbbVie, Dermira, Eli Lilly, Novartis, Oneness Biotech, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Sanofi – investigator; AbbVie, Eli Lilly, Novartis, Pfizer, Roche, Sanofi – consultant; AbbVie, Eli Lilly, Mylan, Novartis, Pfizer, Roche, Sanofi – speaker; Mylan, Pfizer, Roche, Sanofi – advisory board member. Al-Ahmad M: AstraZeneca, GSK, Novartis, Sanofi – advisory board member and speaker. Holzer G: AbbVie, Almirall, Galderma, LEO Pharma, Lilly, Sanofi – advisory board member. Lapeere H: AbbVie, Eli Lilly, LEO Pharma, Pfizer, Sanofi – advisory board member. Čelakovská J: Nothing to disclose. Calzavara-Pinton P: AbbVie, Almirall, Galderma, LEO Pharma, Meda, Sanofi – advisory board member. Ferrucci SM: AbbVie, Eli Lilly, Sanofi, Amgen, Novartis, Galderma – principal investigator; Novartis – advisory board member; Almirall, Menarini, Novartis – honoraria for lectures and research grants.

000182 | Oncostatin M promotes sensory nerve fiber outgrowth

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Background: Atopic dermatitis (AD) is hypersensitive to itching stimuli, and this sensory abnormality is thought to be partly due to an increase in peripheral nerves within the epidermis. Oncostatin M (OSM) is increased in AD lesions, but the influence of OSM on the pathogenesis of AD remains unclear. Signalling of OSM occurs mainly via receptors composed of OSMRβ and gp130 subunits. OSM and IL-31 share a common receptor chain of OSMRβ, and OSM, like

IL-31, may be involved in perceptual abnormalities in the pathogenesis of AD. In this study, we investigated the influence of OSM on the morphology of dorsal root ganglion cells (DRGs), which are afferent sensory nerves.

Method: We investigated whether OSM promotes the elongation of nerve fibres in the DRG. To further clarify that the elongation is caused by signals downstream of OSM, OSM-stimulated nerve elongation was measured after treating DRG cells with inhibitors of intracellular signalling by OSM. OSMRβ-overexpressing DRG cell lines were then established by gene transfer, and OSM-stimulated nerve elongation was measured.

Results: Primary sensory neurons from the dorsal root ganglion (DRG) of mice were treated with OSM and showed neurite outgrowth. Pre-treatment with inhibitors of ERK, STAT3, JNK and p38 followed by OSM inhibited neurite outgrowth, indicating the involvement of JAK/STAT3, MEK/ERK and p38/MAPK signalling in OSM-induced neurite outgrowth. A DRG cell line overexpressing OSMRβ was generated by gene transfer into a mouse DRG cell line (MED17.11). When these cells were treated with OSM, a predominant neurite outgrowth was observed compared to the wild type.

Conclusion: It was speculated that increased OSM in the lesion of AD contributes to itching hypersensitivity through the elongation and increase of afferent sensory nerve fibres in the skin.

Conflicts of interest: The authors did not specify any links of interest.

000843 | Childhood atopic dermatitis is associated with cardiovascular risk factors in young adulhood – A population-based cohort study

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Background: Studies have indicated that atopic dermatitis (AD) is associated with increased risk of cardiovascular disease. However, results are conflicting. Furthermore, a long-term influence of childhood AD on cardiovascular risk factors in young adulthood is less investigated. Therefore, our aim was to assess the associations between AD in childhood and cardiovascular risk factors in young adulthood.

Method: The study encompasses longitudinal data from the Swedish population-based birth cohort BAMSE. Participants with data up to age 24 years were included ($n = 2,270$). The primary outcomes were body mass index (BMI), waist circumference (WC), body fat percent (BF%) measured by bioelectric impedance analysis and blood pressure at 24 years. Secondary outcome was blood lipids. Severe AD was defined as, AD in combination with sleep disturbance (sometimes, often, always) due to itching, obtained from questionnaire.

Results: In total, 18.6% ($n = 420$) had AD at 24 years. Linear regression analyses showed that males with AD had higher BMI ($\beta_{Adj.}$ 0.81, 95% CI 0.15–1.47), BF% ($\beta_{Adj.}$ 1.19, 95% CI 0.09–2.29), systolic blood pressure ($\beta_{Adj.}$ 1.92, 95% CI 0.02–3.82), total cholesterol ($\beta_{Adj.}$ 0.14, 95% CI 0.00–0.28) and LDL cholesterol ($\beta_{Adj.}$ 0.15, 95% CI 0.02–0.27) compared with males without AD. No such associations were seen in females.

Current AD with prepubertal onset was associated with increased BMI in both males ($\beta_{Adj.}$ 0.89, 95% CI 0.11–1.67) and females ($\beta_{Adj.}$ 0.72, 95% CI 0.11–1.33).

At 24 years, 23.1% ($n = 97$) of AD cases fulfilled the criteria for severe AD, which was significantly associated with overweight, with higher BF% (females $\beta_{Adj.}$ 2.49, 95% CI 0.60–4.39, males $\beta_{Adj.}$ 2.96, 95% CI 0.23–5.69) in both sexes, and in females with higher BMI ($\beta_{Adj.}$ 1.83, 95% CI 0.72–2.94) and larger WC ($\beta_{Adj.}$ 4.03, 95% CI 1.54–6.52) compared with peers with mild to moderate AD. No association was seen for the other outcomes.

Conclusion: AD in males appears to be associated with risk factors for cardiovascular disease in young adulthood. The duration and severity of AD seem to be of importance in both sexes.

Conflicts of interest: EKJ has received speaker honoraria and/or been a consultant for AbbVie, ACO, Galenica LEO Pharma, Novartis and Sanofi-Genzyme. SL has been part of the advisory board at Sanofi-Genzyme.

001138 | Longitudinal integrated proteomic and metabolomic skin improvements in atopic dermatitis patients treated with dupilumab

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Background: Inhibition of IL-4/IL-13 driven inflammation by dupilumab has shown significant clinical benefits in treatment of atopic dermatitis (AD). To date, however, the details about the ongoing proteomic and metabolic skin changes in AD patients during dupilumab treatment have not been established.

Method: Skin tape strips (STS) were collected from lesional and non-lesional skin of 20 AD patients over the course of 16 weeks of dupilumab treatment and from 20 healthy volunteers followed for 16 weeks. STS extracts were examined at baseline, weeks 8 and 16 of treatment by liquid chromatography mass spectrometry for proteomic analysis and targeted metabolomics.

Results: 490 proteins were detected in ≥80% of AD and healthy skin samples. 139 of these proteins were differentially expressed in AD STS extracts at baseline in an unsupervised cluster analysis: 90 proteins were significantly increased (cluster 1) and 49 were significantly reduced (cluster 2) in AD skin compared to healthy controls (both $p < 0.0001$). Functionally, cluster 1 (increased in AD) was enriched for markers of epidermal hyperplasia, glycolytic proteins, proteins involved in actin filament organization and protein translation. Cluster 2 (decreased in AD) included proteins involved in epidermal barrier formation, lysosomal enzymes required for lamellae assembly, oxidative response enzymes and proteasome subunits. The expression of cluster 1 and 2 proteins significantly changed during the course of dupilumab treatment, with the significant inhibition of cluster 1 and significant increase in cluster 2 proteins expression by 16 weeks of treatment ($p = 0.0001$ and $p < 0.001$, compared to baseline, respectively) and approached levels observed in healthy skin. These changes were also revealed in differential metabolite changes in corresponding STS extracts. Guanosine, cytidine and their breakdown products guanine, cytosine, xanthine and hypoxanthine were increased in AD lesional STS prior to treatment ($p < 0.0001$ compared to healthy skin). Significant reductions in these metabolites as a reflection of inhibition of transcriptional activity and hyperplasia in AD skin were observed by 16 weeks of dupilumab treatment ($p < 0.01$ to $p < 0.0001$, compared to baseline).

Conclusion: Longitudinal integrated assessment of the skin proteome and metabolome in AD patients treated with dupilumab established significant inhibition of epidermal hyperplasia and improvement in epidermal differentiation by 16 weeks of treatment.

Conflicts of interest: AZ, SB, IA are employees of SanofiThe study was funded by the grant from Sanofi.

000879 | Oncostatin m inhibits IL-31-induced scratching behaviour in mice

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Background: Atopic dermatitis (AD) shows dermatitis, impaired stratum corneum barrier function and pruritus caused mainly by type 2 inflammation such as IL-4,13,31. IL31 is particularly implicated in pruritic skin. Besides type 2 inflammation, oncostatin M (OSM) is also increased in AD lesions, but the role of OSM in the pathogenesis of AD is unknown. This study aims to elucidate the mechanisms by which OSM is increased in AD lesions and to clarify the impact of OSM on the pathogenesis of AD.

Method: Human peripheral blood-derived monocytes were stimulated with various cytokines and the conditions under which they express OSM were investigated.

OSM was administered to mice intravenously and changes in gene expression of cytokine receptors in the skin and dorsal root ganglia (DRG) were investigated.

The effects of OSM on the scratching behaviour of mice in response to various pruritogenic substances were also investigated.

Results: Human monocyte expression of OSM was up-regulated by stimulation with IL-4 and GM-CSF, and co-stimulation with IL-4 and GM-CSF synergistically increased OSM expression. Transvenous administration of OSM increased gene expression of Osmr, Il4ra, Il13ra1, Il13ra2 and Il2rg in mouse DRGs, while Il31ra was decreased. However, there was little effect on the expression of histamine 1 and 4 receptors or transient receptor potential (TRP) channels. In mouse skin, there was no reduction in Il31ra expression by OSM stimulation. OSM did not affect scratching behaviour in response to histamine, but inhibited IL-31-induced scratching behaviour. This suppression of scratching behaviour may be due to the suppression of Il31ra expression in the DRG by OSM.

Conclusion: IL-4 enhanced OSM production from monocytes by co-stimulation with GM-CSF. This OSM might reduce the response to IL-31, while promoting the response to IL-4 and IL13.

Conflicts of interest: The authors did not specify any links of interest.

001640 | Successful dupilumab dose reduction in persistently controlled atopic dermatitis patients

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Background: The efficacy of dupilumab in the treatment of atopic dermatitis (AD) is well established. However, evidence on dose reduction in well-controlled AD is still lacking. We aim to evaluate the efficacy and safety of dupilumab dose reduction in a Portuguese cohort of AD patients.

Method: Retrospective analysis of patients with AD taking dupilumab between January 2020 and January 2023. Atopic comorbidities, serum immunoglobulin E (IgE), serum eosinophil count, disease severity scores, and dupilumab regimens were analysed.

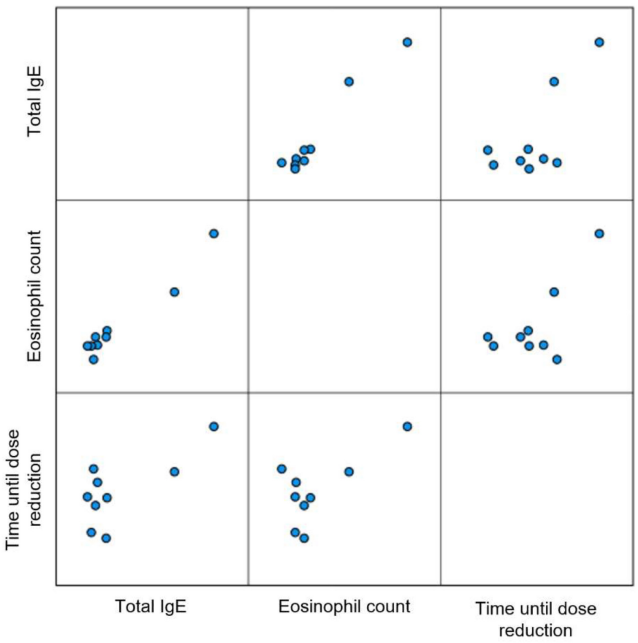
Results: Twenty-one patients were included (mean age 25 years; 38.1% women). All cases started dupilumab with the standard dose (18 with 300mg every 2 weeks, and 3 children with age-related dose adjustments). Based on clinical criteria (SCORAD < 20 and EASI < 7 for at least 4 consecutive weeks), dose reduction was undertaken in 10 patients (47.6%). It was achieved by increasing the original interval to 3 weeks. 4 patients (19.0%) further increased the interval to 4 weeks and 3 patients (14.3%) to 5 weeks. No children achieved dose reduction.

Interval adjustment began 66.1 ± 33.9 weeks after treatment initiation. Disease severity was assessed at least 4 weeks after regimen alteration. Dose reduction did not impair dupilumab effectiveness. All patients maintained disease control with median SCORAD 3.85

(IQR = 0–8.95) and median EASI 0.05 (IQR = 0–0.48). No patient stepped back to the previous dosage.

The time until dose reduction correlated with total serum IgE ($R = 0.724$; $p = 0.027$) and eosinophil count ($R = 0.689$; $p = 0.04$). There was no correlation between reaching criteria for dose reduction and atopic comorbidities, or basal disease scores.

Conclusion: Our study shows that dose reduction was safe and successful in a subgroup of patients with persistently controlled AD while maintaining disease control. We reduced treatment costs by at least 33%, which ultimately increased its cost-effectiveness. In our population, higher serum IgE and eosinophil counts were associated with longer periods until dose reduction. Although limited by the sample size, our data supports dupilumab dose reduction based on clinical criteria.



Conflicts of interest: The authors did not specify any links of interest.

000402 | Disease severity and prior treatment usage in patients with atopic dermatitis initiating dupilumab: An update from the GLOBOSTAD observational study

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*Presenting author: S. M. Ferrucci

Background: The efficacy and safety of dupilumab have been reported previously based on data from controlled clinical trials. The GLOBOSTAD study adds to the existing body of evidence by providing data from a real-world setting. This interim analysis reports prior medication use and disease severity in patients with atopic dermatitis (AD) who received treatment with dupilumab in a real-world setting.

Method: This 5-year, international, multicenter, noninterventional observational study (GLOBOSTAD; NCT03992417) included patients ≥12 years old with AD who initiated dupilumab treatment based on country-specific prescribing information. Data reported are for the population at baseline ($N = 952$, data cutoff: March 2022).

Results: At study entry, mean (standard deviation, SD) SCOring Atopic Dermatitis (SCORAD) score was 60.5 (16.3), of range 0–103 (severe disease: > 50), with a mean affected body surface area of 44.8% (24.4), and an intensity score (range 0–18) of 11.0 (3.3) based on the summative assessment of erythema, edema/papulation, excoriations, lichenification, oozing/crusts and dryness (each range 0–3). A large proportion of patients were in the severe SCORAD category (75.4%), with the rest being in either moderate (22.3%) or mild (2.2%) categories. Within SCORAD, patient-scored visual analog scales (range 0–10) indicated that the mean (SD) pruritus score was 7.2 (2.3) and sleep loss score was 5.8 (3.0). Mean (SD) Dermatology Life Quality Index (DLQI) for adults was 13.7 (7.0) and Children's (C) DLQI for adolescents was 14.4 (5.7), from range 0–30 (very large effect: > 10). 44.0% of adults and 50.0% of adolescents reported that AD had a very large effect on their quality of life. 23.9% and 37.5%, respectively reported a moderate effect, 19.2% and 12.5% an extremely large effect, and 11.2% and 0.0% a small effect. Within the 12 months preceding dupilumab initiation, patients reported use of systemic nonsteroidal immunosuppressants (32.6%), systemic corticosteroids (17.8%), topical corticosteroids (47.2%), topical calcineurin inhibitors (14.8%), and ultraviolet phototherapy (3.4%).

Conclusion: At baseline, the majority of patients enrolled in the GLOBOSTAD study had severe disease, as measured with SCORAD, despite use of various systemic and nonsystemic therapies. Overall, quality of life was considerably impacted (very large effect, as measured by DLQI or CDLQI).

Conflicts of interest: Ardeleanu M: Regeneron Pharmaceuticals Inc. – employee and shareholder. Wu J, Bosman K: Sanofi – employees, may hold stock and/or stock options in the company. Fougerousse AC: AbbVie, LEO Pharma, Lilly, Pfizer, Sanofi – consultant. Tzellos T: AbbVie, LEO Pharma, Pfizer, Sanofi, UCB – grants and personal fees. Chung WH: Nothing to disclose. Lapeere H: AbbVie, Eli Lilly, LEO Pharma, Pfizer, Sanofi – advisory board member. Fomina DS: CSL Behring, Novartis, Sanofi, Shire - honoraria. Rossi M: AbbVie, Cantabria Labs, Novartis, Sanofi – fee and advisory board meetings. Ferrucci SM: AbbVie, Eli Lilly, Sanofi – principal investigator; Novartis – advisory board member; Almirall, Menarini, Novartis – honoraria for lectures and research grants.

000339 | Impact of self-reported comorbid food allergy on efficacy and safety of abrocitinib and dupilumab in patients with moderate-to-severe atopic dermatitis: A pooled analysis of JADE COMPARE and JADE DARE

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Background: Food allergies are common in patients with atopic dermatitis (AD). This post hoc analysis assessed the efficacy and safety of abrocitinib and dupilumab in patients with moderate-to-severe AD, with or without comorbid food allergies.

Method: Data were pooled from adult patients treated with abrocitinib (200 mg QD) or dupilumab (300 mg Q2W) in the phase 3 JADE COMPARE (NCT03720470) and JADE DARE (NCT04345367) trials and were stratified by self-reported food allergy status at baseline. Assessments through week 16 were the proportion of patients achieving an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with ≥2-point improvement, ≥75% improvement in Eczema Area and Severity Index (EASI-75), and ≥4-point improvement in Peak Pruritus Numerical Rating Scale (PP-NRS4); the least squares mean in Dermatology Life Quality Index (DLQI) and SCORing Atopic Dermatitis (SCORAD); the proportion of patients with eosinophilia or hypereosinophilia (counts >500/mm^3); and safety.

Results: Of 1195 pooled patients (abrocitinib: 588; dupilumab: 607), 225 (19%) reported food allergy at baseline. Regardless of comorbid food allergy, comparable proportions of patients achieved improvements in AD signs and symptoms with abrocitinib (IGA 0/1: 53%/53% [with/without food allergy]; EASI-75: 80%/75%; PP-NRS4: 66%/67%) or dupilumab (IGA 0/1: 47%/41%; EASI-75: 72%/68%; PP-NRS4: 64%/62%) at week 16. DLQI and SCORAD improvements with abrocitinib and dupilumab were also comparable between patients with and without food allergy. Regardless of food allergy status, the proportion of patients with eosinophilia or hypereosinophilia rapidly decreased with abrocitinib, a change that was sustained through week 16 (baseline: 39%/24% [with/without food allergy]; week 2: 20%/9%; week 16: 12%/9%) but did not decrease with dupilumab (baseline: 32%/24%; week 2: 32%/21%; week 16: 33%/24%). Treatment-emergent adverse events (TEAEs) occurred in 78%/67% (with/without food allergy) of abrocitinib-treated patients and 62%/59% of dupilumab-treated patients; the occurrence of serious TEAEs was similar across subgroups and treatment arms (abrocitinib: 0.9%/1.5%; dupilumab: 0.9%/1.4%).

Conclusion: Abrocitinib and dupilumab improved the signs and symptoms, as well as quality of life, of patients with moderate-to-severe AD and had a manageable safety profile irrespective of food allergy status. Moreover, abrocitinib, but not dupilumab, decreased eosinophilia and hypereosinophilia regardless of comorbid food allergy.

Conflicts of interest: BG has worked as a consultant for Pfizer Inc.; Genentech and as a speaker/consultant for Regeneron, Sanofi Genzyme, CSL Behring, and Horizon Therapeutics and is on advisory boards for Novartis and Shire. AN is a consultant for Pfizer Inc., AbbVie, Eli Lilly and Company, Galderma, LEO Pharma, Novartis, and Sanofi; is on advisory boards for Pfizer Inc., AbbVie, LEO Pharma, and Sanofi; is an investigator for AbbVie, Eli Lilly and Company, Incyte, LEO Pharma, Novartis, and Sanofi; and is a speaker for AbbVie, Regeneron, and Sanofi. MB has received research grants from Regeneron and is on advisory boards for Pfizer Inc., AbbVie, Eli Lilly and Company, Incyte, Janssen, LEO Pharma, Regeneron, and Sanofi Genzyme. CV is an investigator, speaker, and/or advisor for AbbVie, Eli Lilly and Company, LEO Pharma, Novartis, Pierre Fabre, and Sanofi Genzyme. IL is an employee of IQVIA, paid contractors to Pfizer Inc. in the development of this poster and in statistical support. CF, FJR, HK, and IHM are employees and shareholders of Pfizer Inc.

001006 | Drug utilization among young adults with atopic dermatitis – Gender aspects, level of education and disease severity

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*Presenting author: E. Dahlén

Background: Around 4%–19% of adults are affected by atopic dermatitis (AD). First-line treatment for AD are emollients and topical corticosteroids. There is insufficient knowledge about the drug utilization of young adults with AD and different aspects possibly affecting the drug utilization. Our aim was to describe the drug utilization of young adults with AD and possible differences in the drug dispensing regarding gender, level of education and disease severity.

Method: A cross-sectional study based on the 24-year follow-up from the BAMSE birth cohort linked with dispensing data from the Swedish Prescribed Drug Register ($n = 3055$). AD was defined from questionnaire data. The dispensing patterns of AD drugs were analysed by gender, level of education and disease severity.

Results: The prevalence of AD in young adults was 17.7% ($n = 542$) and 44.8% of them were dispensed at least one drug for the treatment of AD during the study period (January 2016–June 2019). Topical corticosteroids (TCS) were the most common drugs (32.8%) followed by emollients (21.4%). A larger proportion of men was dispensed TCS than women (38.2% vs 29.4%: p-value = 0.03). The proportion of dispensed TCS was smaller for individuals with higher education than those without higher education (26.8% vs 36.5%: $p = 0.02$). A larger proportion of individuals with moderate-to-severe AD was dispensed TCS than individuals with mild AD (53.8% vs 35.6%: p-value = 0.019). Also, among individuals with moderate-to-severe AD, the average amount of TCS dispensed was higher in men compared to women (442 g vs 235 g: p-value = 0.046). The average amount of emollients dispensed was 1706 grams per person during the study period and only 3.1% of the young adults were dispensed ≥ 1000 g per year.

Conclusion: In our population-based cohort, young adults with atopic dermatitis were under-treated or untreated during the study period. Gender, level of education and disease severity did all affect the dispensing patterns of AD drugs.

Conflicts of interest: The authors did not specify any links of interest.

000095 | Effective primary prevention of atopic dermatitis in high-risk neonates via moisturizer application: randomized, blinded, parallel, three-group, Phase II Trial (PAF Study)

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Background: The efficacy of applying moisturizer is inconsistent regarding the primary prevention of atopic dermatitis (AD) based on data from previous RCTs. The most effective moisturizer type and application frequency for preventing infant AD development remain unclear. We previously showed that 2e moisturizer® (Shiseido Japan Co., Ltd., Tokyo, Japan) at least once a day significantly reduced AD onset compared to PROPETO® as needed in young infants (UMIN000004544, JACI 2014). This trial aimed to estimate how effective the twice-daily or once-daily application of Fam's Baby moisturizer® (Fam's Inc., Tokyo, Japan) prevented AD compared to the once-daily application of 2e moisturizer®.

Method: This trial was a single-center, three-parallel group, assessor-blind, superiority, individually randomized, controlled, phase II trial (jRCTs031200070). We randomly assigned sixty newborns with at least one parent or sibling who has had AD to the application of Fam's Baby twice daily (Group A), Fam's Baby once daily (Group B), or 2e once daily (Group C) in a 1:1:1 ratio until 32 weeks old from August 25, 2020 to September 28, 2021. The primary outcome is the time to the onset of AD during the intervention.

Results: We analyzed 60 participants. AD was observed in 11 of 20 infants (55%) in the group A, 5 of 20 (25%) in the group B, and 10 of 20 (50%) in the group C by 32 weeks of age, respectively. Cumulative incidence values for AD by using the Kaplan-Meier method showed that the group B tended to maintain intact skin for longer period than the group C (median time, not reached (NR) vs. 212 days, log-rank test, $p = 0.064$). Cox regression analysis showed the risk of AD tend to be lower in the Group B (hazard ratio with group C as control, 0.36; 95% CI, 0.12–1.06). No serious adverse events occurred in any of the three groups. None were suspected to be related to moisturizer.

Conclusion: Fam's Baby showed more preventive effect than 2e. Further large scale trial will be needed to confirm efficacy of Fam's Baby to prevent AD.

Conflicts of interest: This study received funding from Fam's Inc. (Tokyo, Japan). All authors declare no other competing interests.

Flash talks on angioedema

000899 | Multicentric observational study on safety and tolerability of Covid 19 vaccines in patients with angioedema with C1 inhibitor deficiency: Data from Italian Network on Hereditary and Acquired Angioedema (ITACA)

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*Presenting author: R. Parente

Background: Angioedema with C1 inhibitor deficiency (C1-INH-AE) is a rare disease characterized by recurrent and unpredictable attacks of angioedema without hives, with a heterogeneous phenotypes in terms of severity and site of attacks. The genetic form is a rare autosomal dominant disorder due to C1-inhibitor deficiency (type I) or dysfunction (type II). The acquired form is often associated with hematologic neoplasms or antibodies against C1 inhibitor, causing excessive consumption or inactivation of the protease. In patients with C1-INH-AE, the inadequate control of the contact system causes excessive bradykinin formation with localized and transient increase in vascular permeability, resulting in angioedema attacks. Eliciting factors of the attacks include trauma, emotional factors, medical procedures and infections. Certain studies suggest that mRNA vaccines potentially represent an eliciting factors of angioedema attacks. However, only few data were reported about the safety of COVID-19 vaccines in patients with C1-INH-AE.

Method: In this study we collected the data about a population of 208 adult patients with C1-INH-AE (107 females) followed by 11 reference centers in Italy (Milan, Florence, Padua, Turin, Civitanova Marche, Salerno, Naples, Aosta, Ancona, Genoa, Messina). Of those, the majority of patients (89%) had a diagnosis of hereditary C1-INH-AE and 23 patients were diagnosed as acquired C1-INH-AE. In this cohort the mean attack rate was 0.89/months. Long term prophylaxis (LTP) was prescribed in 80 patients with hereditary C1-INH-AE and in 9 patients with acquired C1-INH-AE. The primary aim of this observational study was to collect data on the onset of acute attacks in the 72 hours following the COVID-19 vaccination.

Results: Between December 2021 and June 2022, 203 patients with C1-INH-AE received Covid 19 vaccines in a controlled medical setting in reference centers. Four hundred and five doses were administered as a part of primary vaccination cycle and 124 doses were given as booster doses. The majority of patients received mRNA vaccines. About 5% of patients received vaccines made using adenovirus vector; in particular ChAdOx1 nCoV-19 vaccines (Astra-Zeneca) and Ad26.COV.2.S (Jassen/Johnson & Johnson). A total of 48 attacks of angioedema occurred within 72 hours after the vaccine administration were registered. The majority of them (50%) were abdominal attacks; extremities were involved in 20% and 39% of cases respectively after primary vaccination cycle and booster doses; combined (cutaneous and abdominal) attacks were occurred respectively in 20% and 11% cases. Three patient reported a laringeal attacks after the administration of first dose of Pfizer (in two cases) and of second dose (in one case). However, no hospitalization was required. In all cases, the attacks were successfully treated with icatibant or plasma derived C1-inhibitor. Interestingly, there is no difference in the rate of attacks occurred after vaccines between patients on LTP regimen and those using on demand treatment.

Conclusion: Our data suggest that Covid 19 vaccines are safe and tolerable in patients with C1-INH-AE. These patients could be vaccinated with these novel vaccines in a controlled medical setting. However, the observational nature of this study and the lack of a control group does not allow the generalization of these results.

Conflicts of interest: The authors did not specify any links of interest.

001008 | Efficacy and safety of lanadelumab in pediatric patients aged 2 to 12

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Background: Symptoms of hereditary angioedema (HAE) often present during childhood, and there is an unmet need for long-term prophylactic (LTP) treatment for patients <12 years old. The SPRING Study (NCT04070326) demonstrated safety and efficacy of lanadelumab in patients 2 to <12 years old that were consistent with those in patients ≥12 years old in previous lanadelumab studies. Here, we compared outcomes in subgroups of patients in SPRING.

Method: Patients with HAE type I/II and a baseline HAE attack rate of ≥1 attack/3 months were enrolled and received lanadelumab

150 mg treatment subcutaneously for 52 weeks. Patients aged 2 to <6 years were treated every 4 weeks (Q4W) and patients 6 to <12 years were treated every 2 weeks (Q2W) but were eligible to switch to Q4W if they were attack-free for 26 weeks. Efficacy in subgroups was analysed based on reduction of HAE attack rate (attacks/month) during treatment. Patients were assigned to subgroups by age, body mass index, sex, baseline attack rate, history of laryngeal attacks, and prior use of LTP, and efficacy and safety were compared for each subgroup.

Results: A total of 21 patients were enrolled in the study. The mean reduction in attack rate from baseline was similar in patients aged 2 to <6 years (96.4%, $n=4$) and 6 to <12 years (94.4%, $n=17$). Attack rate reduction was comparable in subgroups of body mass index (100.0% in underweight [$n=1$]; 95.4% in healthy or overweight [$n=15$]; 91.8% in obese [$n=5$]), sex (90.0% in males [$n=9$]; 98.4% in females [$n=12$]), baseline attack rate (92.8% in >0 to <1 attacks/month [$n=9$]; 98.5% in 1 to <2 attacks/month [$n=7$]; 92.0% in 2 to <3 attacks/month [$n=2$]; 94.1% in ≥3 attacks/month [$n=3$]), history of laryngeal attacks (87.0% in yes [$n=5$]; 97.2% in no [$n=16$]) and prior LTP use (78.3% in C1-INH use [$n=3$]; 97.5% in no LTP [$n=18$]). Overall, there were no discontinuations due to treatment-emergent adverse events (TEAEs) and no serious TEAEs were reported. Severe TEAEs (injection site erythema) were reported for 1 patient. Most TEAEs related to treatment were mild/moderate injection site reactions. There were no clinically meaningful differences in the rate of TEAEs across the subgroups.

Conclusion: Efficacy and safety of lanadelumab in patients aged 2 to <12 years were comparable regardless of age, body mass index, sex, baseline attack rate, and history of laryngeal attacks. The apparent difference with prior LTP use is likely due to small sample size in the C1-INH use group.

Conflicts of interest: IMS has received honoraria, research funding, consultancy fees and travel grants from and/or has participated in advisory boards for BioCryst, CSL Behring, Pharming and Takeda. HF reports receiving research grants from CSL Behring, Shire/Takeda and Pharming and consultancy/ speaker fees and honoraria from BioCryst Pharmaceuticals, Inc., CSL Behring, Pharming Group NV, KalVista and Shire HGT/Takeda and serves as an advisor and principal investigator for clinical trials/ registries for BioCryst Pharmaceuticals, Inc., CSL Behring, Pharming, KalVista and Shire/Takeda. MP reports receiving research grants from CSL Behring, Shire/Takeda and consultancy/ speaker fees and honoraria from CSL Behring and Shire HGT/Takeda and has been an investigator for clinical trials for BioCryst Pharmaceuticals, Inc., CSL Behring, Pharming, and Shire/Takeda MW has nothing to disclose. SR has nothing to disclose. WY has received honoraria for advisory roles and CHE from CSL Behring, Shire/Takeda, BioCryst, and Pharming; has received research grants from CSL Behring, Shire/Takeda, BioCryst, Pharvaris, Pharming, Ionis, Astria, and Intellia; he is a medical advisor (volunteer) for HAE Canada; his clinic is recognized as a Treatment and Reference Centre of Excellence by HAE International -ACARE in Canada JAB has been a clinical investigator for BioCryst, CSL Behring, Pharming, and Takeda; speaker for CSL Behring, Pharming, and Takeda; consultant for BioCryst, CSL Behring, Fresenius Kabi, Kalvista, Pharming, and Takeda; and is an advisory board member of the US Hereditary Angioedema Association. MM is or recently was a speaker and/or adviser for BioCryst, CSL Behring, KalVista, Moxie, Pharming, Pharvaris, and Takeda; and has received research funding from BioCryst, CSL Behring, Moxie, Pharming, and Takeda CN and MY are full-time employees of Takeda and hold stocks/options in Takeda.

001557 | Treatment with oral administered bradykinin B2 receptor inhibitor PHVS416 improves hereditary angioedema attack symptoms

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Background: Excessive activation of bradykinin B2 receptors by bradykinin is the cause of hereditary angioedema (HAE) attacks, manifesting as painful swelling of subcutaneous and submucosal tissue at various body sites. PHA121 is a potent and selective bradykinin B2 receptor antagonist under development for on-demand and prophylactic treatment of HAE.

Method: RAPIDe-1 was a phase 2, double-blind, placebo-controlled, cross-over, dose-ranging trial of PHVS416, oral softgel capsule formulation of PHA121, for treatment of attacks in HAE due to C1INH deficiency. The Mean Symptom Complex Severity (MSCS) score is a measure of attacks' symptom severity incorporating the body sites affected and patient-reported symptom severity at each site. The Treatment Outcome Score (TOS) assesses patient-reported response to therapy based on body sites, baseline severity, and response post-treatment dosing. Change in MSCS [minimally important difference (MID): −0.30] score from pre-treatment to 4 hours (h) post-treatment and TOS (MID: 30) at 4 h post-treatment were secondary endpoints of RAPIDe-1 trial.

Results: Seventy-four participants were enrolled and 62 of them treated 147 qualifying HAE attacks with study drug (PHVS416 10, 20, 30 mg or placebo) at the time of the primary analysis. MSCS (score decreased) and TOS (score increased) improved during the first 4 h after administration of PHVS416 (all 3 doses) whereas they did not significantly change in placebo-treated attacks. At 4 h, the least squares mean differences of change in MSCS and TOS scores in PHVS416 (10, 20, 30 mg)- and placebo-treated attacks were -0.79 (nominal $p < 0.0001$), −0.61 ($p = 0.0008$), and −0.39 ($p = 0.0291$) and 64.13 (nominal $p < 0.0001$), 62.69 ($p < 0.0001$), and 71.06 ($p < 0.0001$), respectively. Estimated median time for patients to achieve improvement ("a little better") for all body sites involved by the attacks at 2 consecutive time points on TOS was 1.89, 2.15, and 1.98 h for PHVS416-treated attacks vs. 7.62 h for placebo-treated attacks. Median time to achieve a status of "a lot better or resolved" at all body sites involved was 4.02, 5.93, and 4.12 h for attacks treated with the 3 doses of PHVS416 vs. 23.28 h for placebo-treated attacks.

Conclusion: In RAPIDe-1 placebo-controlled trial, treatment with PHVS416 led to more rapid symptom relief and resolution of HAE attacks assessed through the MSCS and TOS, consistently with the outcomes of primary and other secondary endpoints measured through the VAS-3.

Conflicts of interest: M. Maurer: has received research grant support and/or speaker/consultancy fees from Adverum, Attune, BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda/Shire.P. Lu: employee of Pharvaris, holds stock options in Pharvaris.A. Lesage: consultant to Pharvaris, holds stocks/stock options in Pharvaris. Advisor to Kosa Pharma, holds stocks in Kosa Pharma.J. Knolle: consultant to Pharvaris, holds stocks/stock options in Pharvaris.L. Zhu: employee of Pharvaris, holds stocks in Pharvaris.H. Chen: employee of Pharvaris, holds stocks in Pharvaris.S. van Leuween: employee of SLC Consultancy and consultant to Pharvaris, holds stocks in Pharvaris.R. Crabbé: employee of CG Consultancy and consultant to Pharvaris, holds stocks in Pharvaris.M.H. Jouvin: employee of Pharvaris, holds stocks in Pharvaris.W.H. Yang: member of advisory boards for BioCryst, CSL Behring, Merck, Novartis, Sanofi, Shire/Takeda; received speaker fees for AstraZeneca, Merck, Novartis, Shire/Takeda; research grants from Aimmune Therapeutics, ALK, AnaptysBio, AstraZeneca, BioCryst Pharmaceuticals, CSL Behring, DBV Technologies, Dermira, Genentech, GlaxoSmithKline, Glenmark, Pharming, Regeneron, Roche, Sanofi, Shire/Takeda.A. Valerieva: received consultant, speaker, and personal fees from Astra Zeneca, Berlin-Chemie/Menarini Group, CSL Behring, Novartis, Pharming Group N. V., Shire/Takeda, SOBI, Teva. Investigator for Pharvaris.M.D. Tarzi: no conflicts of interests to disclose relatively to this work.G.L. Sussman: received grants and personal fees Aimune Amgen, CSL Behring, DBV, Genentech, Green Cross, Kedrion, Leo, Novartis, Sanofi; consulting honararia from Amgen. CSL Behring, Novartis, Novo; non-financial support from Novartis, Novo, Pediapharm, Sanofi.M. Stobiecki: received personal fees from BioCryst, CSL Behring, KalVista, Pharming, Shire/Takeda.P. Staubach: received personal fees and nonfinancial support from CSL Behring, Shire/Takeda; grants, personal fees, and nonfinancial support from Novartis; personal fees from Pfleger.M. Staevska: no conflicts of interests to disclose relatively to this work.G. Spadaro: no conflicts of interests to disclose relatively to this work.B. Ritchie: received research grants from CSL-Behring, participated in clinical trials with BioCryst, CSL-Behring, Ionis, KalVista, Pharvaris, Takeda. M.A. Riedl: received research support from BioCryst, Biomarin, CSL Behring, Ionis, KalVista, Pharvaris, Takeda; consultant to Astria, BioCryst, Biomarin, CSL Behring, Cycle Pharma, Fresenius-Kabi, Ipsen, KalVista, Ono Pharma, Pfizer, Pharming, Pharvaris, RegenexBio, Sanofi-Regeneron, Takeda. Speaker presenter for CSL Behring, Grifols, Pharming, Takeda.A. Reshef: received research grants, speakers and consulting honoraria from BioCryst, CSL Behring, Pharming, Pharvaris, Shire/Takeda, Stallergens, Teva.M.E. Manning: speaker for Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Genentech, GSK, Pharming, Sanofi/Regeneron, Takeda;

advisor/consultant to BioCryst, CSL Behring, Cycle, KalVista, Pharming, Takeda; received research grants from Allakos, BioCryst, CSL Behring, GSK, KalVista, Merck, Novartis, Merck, Pharming, Pharvaris, Takeda.M. Magerl: personal fees and non-financial support from BioCryst, CSL Behring, KalVista, Novartis, Octapharma, Pharming, Shire/Takeda.H.H. Li: Speaker bureau member for BioCryst, CSL Behring, Pharmaing, Takeda. Received research grant/funding for sponsored research from BioCryst, BioMarin, CSL Behring, Intellia, Kalvista, Pharvaris and consultancy fees from BioCryst, BioMarin, CSL Behring, KalVista, Pharming, Takeda.R. Lleonart: received speaker/consulting fees and funding for travel/meeting attendance from CSL Behring, Takeda; participated in clinical trials/registries for BioCryst.P. Králícková: no conflicts of interests to disclose relatively to this work.S. Kiani-Alikhan: Chief and/or principal investigator for studies and in receipt of honorarium for consulting work and advisory boards organised by: BioCryst, Biotest, CSL Behring, Ionis Pharmaceuticals, KalVista, Pharvaris, Shire/Takeda, X4 Pharmaceuticals.A. Kessel: received travel grants from Pharming, Takeda; honoraria from CSL Behring, Takeda.J.S. Jacobs: received consultant fees from BioCryst, CSL Behring, Cycle pharmaceuticals, Pharming, Takeda; honoraria from, BioCryst, Takeda; funding for sponsored research from CSL Behring, Oasis pharmaceuticals, Pharvaris, Takeda.R. Hakl: received consultancy/speaker honoraria from CSL Behring, Shire, and Takeda Pharmaceutical Co. Ltd., and has served as a principal investigator for clinical trials sponsored by BioCryst, CSL Behring, KalVista, Pharvaris Netherlands BV, Pharming.D. Hagin: no conflicts of interests to disclose relatively to this work.M. Guilarte: received honoraria for educational purposes from CSL Behring, Novartis, Takeda; participated in advisory boards organized by CSL Behring, Novartis, Takeda; received funding to attend conferences and educational events from CSL Behring, Novartis, Pharming, Takeda; is a clinical trial/registry investigator for BioCryst, CSL Behring, Novartis, Pharming, Pharvaris, Takeda.J. Greve: received travel grants, research grants, and honoraria for speaking engagements from CSL Behring, Shire/Takeda.H. Farkas: received research grants from CSL Behring, Pharming, Takeda and served as an advisor for these companies and BioCryst, KalVista, ONO Pharmaceutical; has participated in clinical trials/registries for BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda.O. Fain: consultant for BioCryst, CSL Behring, Takeda.A. Du Than: speaker and/or investigator for BioCryst, Takeda.D.M. Cohn: received consultancy fees from BioCryst, CSL Behring, Pharming, Pharvaris, Shire/Takeda.H. Chapdelaine: received grants from CSL Behring, Dyax, Green Cross, Merck, Novartis, Pharvaris, Sanofi, Takeda; personal fees CSL Behring, Sobi, Takeda.L. Bouillet: received fees from BioCryst, Blueprint, CSL Behring, Novartis, Shire/Takeda.M.L. Baeza: received honorary speaker from Behring, Shire HGT; meeting finance from CSL Behring, Shire HGT; consultant to CSL Behring, Shire HGT; investigator in clinical trials for CSL Behring, Shire HGT, BioCryst.J. Anderson: speaker bureau member for CSL Behring, Pharming, BioCryst, Takeda; received consulting fees from and is a clinical trial investigator for BioCryst, BioMarin, CSL Behring, KalVista, Pharming, Pharvaris, Takeda, and consulting fees from Cycle Pharmaceuticals.E. Aygören-Pürsün: received personal fees from BioCryst, Biomarin, Centogene, CSL Behring, KalVista; Pharming, Pharvaris, Shire/Takeda; grants from CSL Behring, Shire/Takeda.

000432 | Mutant plasminogen in hereditary angioedema is bypassing FXII/kallikrein to generate bradykinin

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Background: Hereditary angioedema (HAE) is a potentially fatal disorder resulting in recurrent attacks of severe swelling. It may be associated with a genetic deficiency of functional C1 inhibitor (HAE-C1-INH) or with normal C1-INH (HAEnCI). In families with HAEnCI, HAE-linked mutations in the *F12*, *PLG*, *KNG1*, *ANGPT1*, *MYOF* and *HS3ST6* genes have been identified. The release of bradykinin from kininogen via the kallikrein-kinin system (KKS) has been shown to be the main mediator in HAE-FXII, but for HAE-PLG there are only first indications how the *PLG* mutations can result in bradykinin release.

Method: Probands of this study comprised eight individuals of one four-generation family with HAE-PLG. Methods comprised biochemical analysis of C1-INH and coagulation systems, protein assays for analyzing the cleavage of high molecular weight kininogen by wild-type and mutant plasminogen and structural analysis of the mutant protein.

Results: In this family we identified an additional *F12* mutation, resulting in the loss of one *F12* allele. There were no differences in the clinical presentation between HAE-PLG patients with and without the additional *F12* mutation, thus we concluded that the KKS is bypassed in HAE-PLG. We could confirm the gain of function by the p.K330E mutation *in vitro* using purified HMWK which we incubated with purified wild type respectively mutant plasminogen. Mutant plasminogen did not only cleave HMWK more efficiently, but also resulted in an increased bradykinin production compared to wild type plasminogen. We observed more intense signals at the bradykinin mass in the mutant plasminogen group in all experiments. Structural modeling and *in vitro* assays using purified proteins confirmed the *PLG* mutation c.988A>G; p.K330E to be a gain of function mutation resulting in an increased bradykinin release by direct cleavage of HMWK.

Conclusion: In summary, the clinical, structural, and biochemical data lead us to the conclusion that the HAE-causing plasminogen

mutation p.K330E results in a gain of function, which enables mutant plasminogen to cleave HMWK more efficiently than the wild-type and produce a critical amount of bradykinin by bypassing FXII/kallikrein.

Conflicts of interest: The authors did not specify any links of interest.

000786 | Real-world effectiveness of lanadelumab in European patients with HAE type I/II: Results from the retrospective integrated study

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Background: Lanadelumab, a fully human monoclonal antibody and inhibitor of plasma kallikrein, is approved in several countries to prevent recurrent hereditary angioedema (HAE) attacks in patients ≥12 years. In Europe, the recommended starting dose of lanadelumab is 300 mg every 2 weeks (Q2W), though this dose can be reduced to every 4 weeks (Q4W) for patients who are stably attack-free on treatment. This study assessed the effectiveness and dose adaptation with lanadelumab in preventing HAE attacks in a real-world setting.

Method: This was a real-world, European (Germany, France, Austria, Greece), retrospective chart review study of patients ≥12 years old with HAE type I or II who initiated long-term prophylaxis (LTP) with lanadelumab from 14 November 2017 to 31 October 2021. Data were collected from lanadelumab initiation (index event) to earliest of discontinuation, death, loss to follow-up, or chart abstraction initiation. Medical and HAE treatment history were collected for 12 months pre-index. Documentation of attacks in the medical chart/diary was required pre-index and post-index. Primary outcomes included effectiveness of lanadelumab on cumulative and per-person month attack-free rate (AFR) and the effect of dose interval increase from Q2W on the AFR.

Results: The analysis included 198 patients treated with lanadelumab (Germany $n = 76$, France $n = 86$, Austria $n = 14$, Greece $n = 22$): 182 (91.9%) with type I HAE and 16 (8.1%) with type II HAE. Mean (SD) age was 43.4 (15.7) years, 61.6% were female and 30.8% had a history of life-threatening attacks. Overall, 59.6% received prior ≥1 LTP and 99.0% on-demand treatments. The mean (SD) pre-index number of attacks was 35.8 (33.2) over 12 months. From index, the median treatment duration was 28.8 months (IQR:20.4-35.7); 96% of patients were still treated with lanadelumab at the end of data collection;144 (72.7%) patients had ≥1 increase in interval of administration with mean (SD) of 8.1 (6.3) months to first increase in interval from Q2W. While monthly AFRs varied from 16.2% to 28.3% during the pre-index period, they ranged from 82.7% and 84.8% (months 1 and 2) to >95% (months 26, 36, 38, 39, and 41+) post-index. No patients had life-threatening attacks post-index.

Conclusion: The final analysis suggests that lanadelumab LTP considerably improves AFRs. The study also provides real-world insight into utilization patterns, specifically that physicians are individualizing lanadelumab treatment by increasing the intervals of administration in clinical practice.

Conflicts of interest: LS is an employee of PPD, part of Thermo Fisher Scientific, Canada.FG, IA and NBE are employees of Takeda and own Takeda stocks. IMS has received honoraria, research funding, consultancy fees, and travel grants from and/or has participated in advisory boards for BioCryst, CSL Behring, Pharming, and Shire (a Takeda company). LB has received honoraria and travel grants from CSL Behring, Novartis, Pharming, and Takeda, and his institute has received research funding from CSL Behring, Novartis, and Takeda. MM has received research grant support and/or speaker/consultancy fees from BioCryst, CSL Behring, KalVista, Pharming, and Shire (a Takeda company).

000626 | A global consensus on the definition, acronyms, nomenclature, and classification of angioedema (The DANCE initiative)

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Background: Angioedema (AE) is a global and common problem. Many patients with AE experience a long delay in diagnosis, and the rate of misdiagnosis is high. By definition, all AEs are associated with increased vascular permeability. However, they are clinically heterogeneous, can occur only once or be recurrent, with or without wheals, be hereditary or acquired, due to mast cell mediators or bradykinin. Recently, new pathogenetic mechanisms were reported, novel AE-driving mutations were described, and many medications were implicated with AE. Therefore, an updated classification may better profile AE types and subtypes, and assist in future personalized medicine. Currently, different taxonomic systems are being used, which makes it difficult to compare the results of studies, develop multicenter collaboration, and harmonize the care for AE patients. The DANCE initiative aims to change this, with the development and publication of a global consensus on the definition, acronyms, nomenclature, and classification of AE.

Method: A focused literature search examined publications on AE types, definitions, and classifications. A steering committee ($n = 13$) agreed on the aims, rationale, and principles of a new and global definition, classification and terminology of AE. Subsequently, international AE experts were presented with statements and a vocabulary

of acronyms for all AE types and subtypes. Consensus, defined as ≥75% agreement, was reached by discussion and voting using an online DELPHI process. The DANCE initiative is supported and endorsed by several global organizations and societies of allergy, immunology, and dermatology.

Results: Ninety-two experts from 35 countries participated in this global initiative. Five rounds of consensus finding were completed by the steering committee, followed by 3 rounds of voting by the global experts, over 16 months (June 2021 to November 2022). The rate of agreement across 19 statements ranged from 83% to 100%. The new classification is based on endotypes and includes revised acronyms for all types of AEs. A consensus document will be published, including expert comments, discussing and supporting each statement.

Conclusion: The DANCE initiative resulted in an international consensus on the classification and terminology of a wide range of AE. The new AE taxonomy and nomenclature will harmonize and facilitate AE research, clinical studies, and patient care.

Conflicts of interest: The authors did not specify any links of interest.

001510 | Efficacy and safety of oral administered bradykinin B2 receptor inhibitor PHVS416 in treatment of hereditary angioedema attacks: Topline results of RAPIDE-1 phase 2 trial

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Background: Swelling attacks of hereditary angioedema (HAE) are caused by excessive bradykinin activating the bradykinin B2 receptor (B2R). PHA121, a potent, selective B2R antagonist, is under development for on-demand and prophylactic treatment of HAE.

Method: RAPIDe-1 was a phase 2, double-blind, placebo-controlled, cross-over, dose-ranging trial of PHVS416, oral softgel capsule formulation of PHA121, for treatment of attacks in HAE due to C1INH deficiency. Seventy-four participants aged ≥18 and ≤75 years, diagnosed with HAE-1 or -2, with ≥3 attacks in the last 4 months or ≥2 attacks in the last 2 months prior to screening, were enrolled from approx. 30 Sites in Canada, Europe, Israel, the United Kingdom, and the United States.

Results: The primary analysis included 147 qualifying HAE attacks treated by 62 participants with double-blinded study drug (placebo or PHVS416 10, 20, or 30 mg). Analysis of the primary endpoint showed that PHVS416 significantly reduced attack symptoms measured as change in the mean 3-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score during HAE attacks, at 4 hours vs placebo ($p < 0.0001$; least squares mean difference of VAS-3 change: −16.75, −15.02, and −16.28 for PHVS416 10, 20 and 30 mg, respectively, vs. placebo). Key secondary endpoints were met with PHVS416 significantly reducing time to onset of relief [≥30% reduction in VAS-3; median (hours): 2.1–2.7 for PHVS416 at 3 doses vs. 8.0 for placebo, $p < 0.01$ for all comparisons], time to ≥50% reduction in VAS-3 [median (hours): 3.3–4.0 for

PHVS416 at 3 doses vs. 22.8 for placebo, $p < 0.001$ for all comparisons], and time to almost complete or complete resolution of symptoms [VAS-3 score ≤10; median (hours): 5.8-20.0 for PHVS416 at 3 doses vs. 42.0 for placebo, $p < 0.05$ for all comparisons]. PHVS416 also substantially reduced the use of rescue medication vs. placebo: 18.9%, 10.7%, and 6.5% in attacks treated with PHVS416 10, 20 and 30 mg, respectively, vs. 60.8% in attacks treated with placebo, at 12 hours. PHVS416 was generally well tolerated with 3 treatment-related adverse events (TRAEs) reported for 1 PHVS416 30mg-treated attack (2.8%) and 1 TRAE reported for 1 placebo-treated attack (1.9%).

Conclusion: Results of the primary analysis of the RAPIDe-1 trial provide proof-of-concept and evidence for the efficacy and safety of PHVS416 in treating HAE attacks and support further development of PHVS416 as a potential on-demand therapy for HAE.

Conflicts of interest: M. Maurer: has received research grant support and/or speaker/consultancy fees from Adverum, Attune, BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda/Shire.J. Anderson: speaker bureau member for CSL Behring, Pharming, BioCryst, Takeda; received consulting fees from and is a clinical trial investigator for BioCryst, BioMarin, CSL Behring, KalVista, Pharming, Pharvaris, Takeda, and consulting fees from Cycle Pharmaceuticals.E. Aygören-Pürsün: received personal fees from BioCryst, Biomarin, Centogene, CSL Behring, KalVista; Pharming, Pharvaris, Shire/Takeda; grants from CSL Behring, Shire/Takeda.M.L. Baeza: received honorary speaker from Behring, Shire HGT; meeting finance from CSL Behring, Shire HGT; consultant to CSL Behring, Shire HGT; investigator in clinical trials for CSL Behring, Shire HGT, BioCryst.L. Bouillet: received fees from BioCryst, Blueprint, CSL Behring, Novartis, Shire/Takeda.H. Chapdelaine: received grants from CSL Behring, Dyax, Green Cross, Merck, Novartis, Pharvaris, Sanofi, Takeda; personal fees CSL Behring, Sobi, Takeda.D.M. Cohn: received consultancy fees from BioCryst, CSL Behring, Pharming, Pharvaris, Shire/Takeda.A. Du Than: speaker and/or investigator for BioCryst, Takeda.O. Fain: consultant for BioCryst, CSL Behring, Takeda.H. Farkas: received research grants from CSL Behring, Pharming, Takeda and served as an advisor for these companies and BioCryst, KalVista, ONO Pharmaceutical; has participated in clinical trials/registries for BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda.J. Greve: received travel grants, research grants, and honoraria for speaking engagements from CSL Behring, Shire/Takeda.M. Guilarte: received honoraria for educational purposes from CSL Behring, Novartis, Takeda; participated in advisory boards organized by CSL Behring, Novartis, Takeda; received funding to attend conferences and educational events from CSL Behring, Novartis, Pharming, Takeda; is a clinical trial/registry investigator for BioCryst, CSL Behring, Novartis, Pharming, Pharvaris, Takeda.D. Hagin: no conflicts of interests to disclose relatively to this work.R. Hakl: received consultancy/speaker honoraria from CSL Behring, Shire, and Takeda Pharmaceutical Co. Ltd., and has served as a principal investigator for clinical trials sponsored by BioCryst, CSL Behring, KalVista, Pharvaris Netherlands BV, Pharming.J.S. Jacobs: received consultant fees from BioCryst, CSL Behring, Cycle pharmaceuticals, Pharming, Takeda; honoraria from, BioCryst, Takeda; funding for sponsored research from CSL Behring, Oasis pharmaceuticals, Pharvaris, Takeda.A. Kessel: received travel grants from Pharming, Takeda; honoraria from CSL Behring, Takeda.S. Kiani-Alikhan: Chief and/or principal investigator for studies and in receipt of honorarium for consulting work and advisory boards organised by: BioCryst, Biotest, CSL Behring, Ionis Pharmaceuticals, KalVista, Pharvaris, Shire/Takeda, X4 Pharmaceuticals.P. Králícková: no conflicts of interests to disclose relatively to this work.R. Lleonart: received speaker/consulting fees and funding for travel/meeting attendance from CSL Behring, Takeda; participated in clinical trials/registries for BioCryst.H.H. Li: Speaker bureau member for BioCryst, CSL Behring, Pharmaing, Takeda. Received research grant/funding for sponsored research from BioCryst, BioMarin, CSL Behring, Intellia, Kalvista, Pharvaris and consultancy fees from BioCryst, BioMarin, CSL Behring, KalVista, Pharming, Takeda.M. Magerl: personal fees and non-financial support from BioCryst, CSL Behring, KalVista, Novartis, Octapharma, Pharming, Shire/Takeda.M.E. Manning: speaker for Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Genentech, GSK, Pharming, Sanofi/Regeneron, Takeda; advisor/consultant to BioCryst, CSL Behring, Cycle, KalVista, Pharming, Takeda; received research grants from Allakos, BioCryst, CSL Behring, GSK, KalVista, Merck, Novartis, Merck, Pharming, Pharvaris, Takeda.A. Reshef: received research grants, speakers and consulting honoraria from BioCryst, CSL Behring, Pharming, Pharvaris, Shire/Takeda, Stallergens, Teva.M. Staevska: no conflicts of interests to disclose relatively to this work.P. Staubach: received personal fees and non-financial support from CSL Behring, Shire/Takeda; grants, personal fees, and nonfinancial support from Novartis; personal fees from Pfleger.M. Stobiecki: received personal fees from BioCryst, CSL Behring, KalVista, Pharming, Shire/Takeda.G. Spadaro: no conflicts of interests to disclose relatively to this work.B. Ritchie: received research grants from CSL-Behring, participated in clinical trials with BioCryst, CSL-Behring, Ionis, KalVista, Pharvaris, Takeda.M.A. Riedl: received research support from BioCryst, Biomarin, CSL Behring, Ionis, KalVista, Pharvaris, Takeda; consultant to Astria, BioCryst, Biomarin, CSL Behring, Cycle Pharma, Fresenius-Kabi, Ipsen, KalVista, Ono Pharma, Pfizer, Pharming, Pharvaris, RegenexBio, Sanofi-Regeneron, Takeda. Speaker presenter for CSL Behring, Grifols, Pharming, Takeda.P. Lu: employee of Pharvaris, holds stock options in Pharvaris.A. Lesage: consultant to Pharvaris, holds stocks/stock options in Pharvaris. Advisor to Kosa Pharma, holds stocks in Kosa Pharma.J. Knolle: consultant to Pharvaris, holds stocks/stock options in Pharvaris.L. Zhu: employee of Pharvaris, holds stocks in Pharvaris.H. 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BioCryst Pharmaceuticals, CSL Behring, DBV Technologies, Dermira, Genentech, GlaxoSmithKline, Glenmark, Pharming, Regeneron, Roche, Sanofi, Shire/Takeda.A. Valerieva: received consultant, speaker, and personal fees from Astra Zeneca, Berlin-Chemie/Menarini Group, CSL Behring, Novartis, Pharming Group N. V., Shire/Takeda, SOBI, Teva. Investigator for Pharvaris.M.D. Tarzi: no conflicts of interests to disclose relatively to this work.G.L. Sussman: received grants and personal fees Aimune Amgen, CSL Behring, DBV, Genentech, Green Cross, Kedrion, Leo, Novartis, Sanofi; consulting honararia from Amgen. CSL Behring, Novartis, Novo; non-financial support from Novartis, Novo, Pediapharm, Sanofi.

000794 | Real-world burden of illness in patients with hereditary angioedema (HAE) type I and II

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Background: Hereditary angioedema (HAE) is a rare, autosomal dominant inherited disorder with recurrent, painful, unpredictable, and potentially fatal episodes of angioedema. Treatment guidelines* recommend assessing attack frequency, quality of life (QoL) and failure to achieve adequate control with on-demand therapy prior to long-term prophylaxis (LTP). There is a need to understand the real-world burden of HAE and HAE patients' perspective on their QoL.
Method: An observational retrospective cohort study was conducted (2022) in patients aged ≥12 years with inadequately controlled HAE type I or II in 20 European countries, Israel and Canada. Patients using LTP with lanadelumab were excluded. Data was collected via medical chart review, with a 12-month observation period anchored to a qualifying event (QE, the patients' last documented HAE attack within the eligibility period). Further, a one-time cross-sectional patient-reported QoL survey was distributed after enrollment. All data were collected between 05 April 2022 and 30 November 2022. Analyses were descriptive.
Results: Medical charts were abstracted from 214 patients from 32 HAE centers in 20 countries. Patients (58.9% females) were 13–87 years old at the QE, and had a family history of HAE (81.8%). Patients experienced a mean (SD) of 9.9 (13), and a maximum of 73 HAE attacks during the 12-month observation period. Attacks lasted 1.9 days on average (range: 1–16 days), and mostly affected the extremities (71.5%) and abdomen (69.6%). Laryngeal/pharyngeal attacks occurred in 22.0% of patients. In terms of severity, patients experienced mild (64.0%), moderate (76.6%) and severe (45.3%) HAE attacks. A total of 91 (42.5%) patients used LTP; 185 (86.4%) used on-demand treatment with or without LTP. Hospitalisations and emergency room visits occurred in 2.3% and 21.5% of patients, respectively. The angioedema quality of life (AE-QoL) questionnaire was completed by 132 patients ≥18 years. On a scale of 0 to 100 (higher scores indicating worse QoL), the mean (SD) AE-QoL total score was 44.1 (24), indicating moderate to large impairment. Mean (SD) domain scores were 54.0 (29) for fears/shame, 41.9 (29) for functioning, 37.9 (25) for fatigue/mood and 35.3 (28) for nutrition.
Conclusion: This real-world study shows that uncontrolled HAE patients experience mild, moderate and severe attacks, and have impaired QoL. Novel, effective and safe LTP could be beneficial to further reduce HAE burden and optimize patients' QoL.
Conflicts of interest: HF reports receiving research grants from CSL Behring, Shire/Takeda and Pharming and consultancy/speaker fees and honoraria from BioCryst Pharmaceuticals, Inc., CSL Behring, Pharming Group NV, KalVista and Shire HGT/Takeda and serves as an advisor and principal investigator for clinical trials/registries for BioCryst Pharmaceuticals, Inc., CSL Behring, Pharming, KalVista and Shire/Takeda.EAP received grants and/or fees as consultant or speaker for Biocryst, Centogene, CSL Behring, Kalvista, Pharming, Pharvaris and Shire/Takeda. AK research grants from Takeda and BioCryst, served on advisory boards for Takeda, BioCryst, Kalvista and CSL Behring and received speaker fees from Takeda and CSL Behring. FP has received speaker and advisory board funding from Takeda Pharmaceuticals, CSL Behring and principal investigator for clinical trials/registries for CSL Behring, Pharming, KalVista and Shire/Takeda. DGE does not have any disclosure. NB has received research grants from Takeda and Pharming and consultancy/speaker fees and honoraria from Pharming Group NV, KalVista and Shire HGT/Takeda and serves as an advisor and principal investigator for clinical trials for BioCryst Pharmaceuticals, Pharming, KalVista and Shire/Takeda. FG, NBE and IA are employees of Takeda and own Takeda stocks. LS is an employee of PPD, part of Thermo Fisher Scientific, Canada.

000517 | Remaining burden of hereditary angioedema (HAE) attacks despite modern long-term prophylaxis

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Background: HAE is characterized by recurrent, unpredictable episodes of subcutaneous or submucosal swelling which can affect the abdomen, extremities, genitals, face, and larynx. Although long-term prophylactic treatment has improved HAE attack burden, quality of life has not been fully restored for many people living with HAE. This

survey evaluates the patterns of prophylactic treatment and impacts on quality of life, as reported by those living with HAE.

Method: People living with HAE were recruited by the US Hereditary Angioedema Association (HAEA) to complete a 20-minute online survey between September 6, and October 19, 2022. Participants provided informed consent for their data to be used anonymously or in aggregate.

Results: Respondents included 107 participants; 80% female, 98% adults (≥18 yrs). Of these, 54 patients reported being treated with both prophylactic and on-demand treatment. Prophylactic treatments included lanadelumab-flyo (57%), berotralstat (13%), C1 esterase inhibitor [Haegarda] (13%), androgens/steroids (9%), and C1 esterase inhibitor [Cinryze] (7%). Despite being treated with prophylactic treatment, 96% reported that they do not feel as though they are 100% themselves, all of the time. Forty-three percent of those on prophylactic treatment report that they modify their activities and lifestyle in order to avoid potential triggers of an HAE attack. Despite prophylaxis, these patients report that their need for on-demand treatment has impacted their choice of career (53%), where they decide to travel (61%), participation in social activities (57%) and day-to-day work (57%) and school (30%) activities. When an HAE attack occurs, 96% of those on prophylaxis feel that they must change their plans for the day.

Conclusion: Despite the promise of modern prophylactic treatment to decrease the HAE attack burden and allow people with HAE to live normal lives, those on prophylaxis still do not feel as though they are 100% themselves and modify important aspects of their lives to avoid triggering HAE attacks. Overall, people with HAE on modern prophylactic treatment are still compromising the quality of their everyday life.

Conflicts of interest: Teresa Caballero – Advisory Board/Consultant and/or Grant/Research Support: Astria, BioCryst Pharmaceuticals, CSL Behring, KalVista Pharmaceuticals, Inc., Novartis, Pharming, Pharvaris, and Shire/Takeda; researcher from the IdiPAZ Program. Ledia Goga – Employee of KalVista Pharmaceuticals, Inc.Sherry Danese – Consultant fees from KalVista Pharmaceuticals, Inc. Markus Heckmann –Employee of KalVista Pharmaceuticals, Inc.Sally van Kooten –Employee of KalVista Pharmaceuticals, Inc. Stephen Betschel – Speaker/Consultant: CSL Behring, Green Cross, Ionis, Octapharma, and Shire/Takeda, and KalVista Pharmaceuticals, Inc.

000638 | Assesment of endothelial dysfunction in (HAE)

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Background: There are contradictory findings about the involvement of endothelial dysfunction in hereditary angioedema (HAE). Therefore, we aimed to evaluate the endothelial function in patients with HAE in this study.

Method: The study included 35 HAE patients who did not have any other risk factors for the development of endothelial dysfunction and age and gender matched 25 healthy subjects as a control group. Bilateral carotis intima-media thickness (CIMT) and flow mediated dilation (FMD) measurements were performed by single operator. Clinical and demographic features of the patients were obtained from their medical records. Written consent was obtained from all participants.

Results: The median (IQR) age of the patients was 29 (24–34) year and 68.6% were female. 85.7% ($n = 30$) of the patients were diagnosed with type 1 HAE, 8.6% ($n = 3$) type 2 HAE, and 5.7% ($n = 2$) nC1-INH HAE. The mean age at diagnosis was 22 ± 8.3 years. The median age of symptom onset (IQR) was 11 (7–11) year. While 42.9% of the patients were under long-term prophylaxis treatment (LTP) with danazol, 62.9% were under only on demand treatment with C1 inhibitor concentrate or icatibant. The mean disease severity score of the patients was 6.57 ± 1.89. The median FMD % values were significantly lower in HAE patients than the healthy subjects ($p < 0.001$) while both right and left sided median CIMT values were similar ($p > 0.05$). Gender, age, serum C4 and C1 INH levels at the diagnosis, disease severity score, usage of LTP treatment, type of HAE, and attack frequency were not associated with the percentage of FMD ($p > 0.05$). Disease duration was correlated with the decrease in FMD percentage ($r = -0.480$, $p = 0.003$).

Conclusion: Our study indicated the presence of endothelial dysfunction in HAE structurally independent from atherosclerosis. Furthermore, it was determined that endothelial dysfunction can be related to disease duration independent from disease severity. Accordingly, close follow up of these patients can be beneficial in regard to vascular related mortality and morbidity.

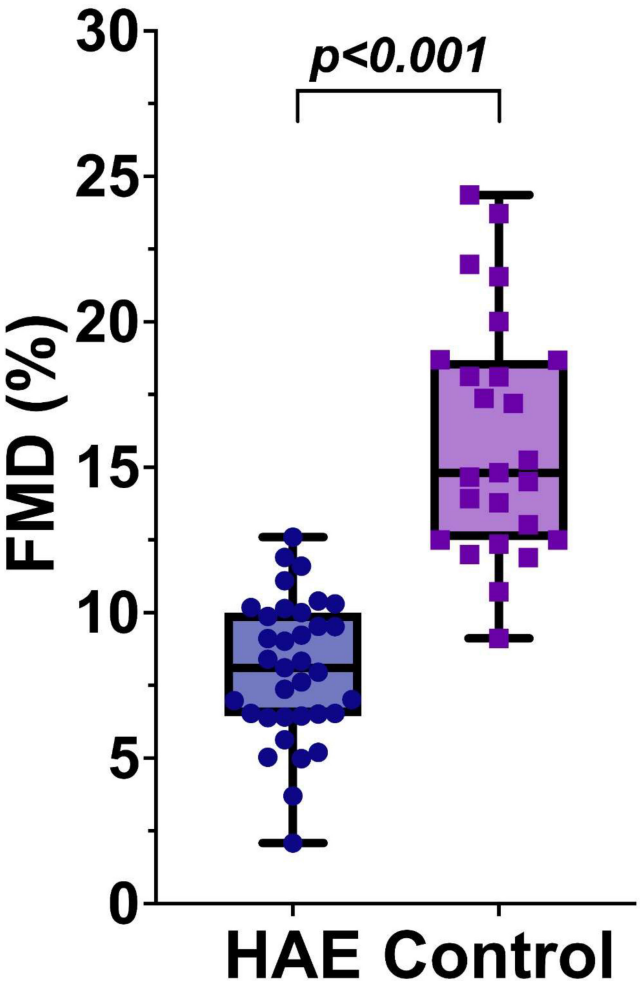

FIGURE 1 FMD difference between HAE and control group. FMD, flow mediated dilation; HAE, hereditary angioedema.

Conflicts of interest: The authors did not specify any links of interest.

001055 | **Burden of (HAE): Findings from a multinational patient survey in Argentina and Colombia**

M. Watt[1]; A. Simon[1]; R. Murphy[2]; M. De La Cruz[2]; D. Romanus[1]; R. Zwiener[3]; M. Sarrazola[4]

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*Presenting author: R. Zwiener

Background: Hereditary angioedema (HAE) is a rare debilitating genetic disorder characterised by recurrent unpredictable, painful, and potentially life-threatening swelling attacks. There are limited data on the variability of HAE, disease burden, and impact on quality of life (QoL) in Latin America.

Method: A non-interventional, cross-sectional, web-based survey was conducted with adult patients in Argentina (ARG) and Colombia (COL) who had self-reported physician diagnoses of HAE, ≥1 attack or prodromal symptom within the past year, and received HAE medication within the last 2 years. Demographic and clinical characteristics of patients and their perspectives on the burden of HAE were collected. Control of disease was assessed using the Angioedema Control Test (AECT; scores ≥10 indicate controlled disease). Health-related QoL was assessed using the Angioedema Quality of Life (AE-QoL; higher scores indicate poorer quality of life) and SF-12 questionnaires. The Hospital Anxiety and Depression Scale (HADS) and Work Productivity and Activity Impairment Questionnaire-General Health (WPAI-GH) questionnaires were also administered.

Results: A total of 70 patients participated in the survey ($n = 45$ ARG [mean age 41.8 years], $n = 25$ COL [mean age 38.4 years]). The majority were female (82% ARG, 64% COL), had HAE type I/II (87% ARG, 88% COL), a family history of HAE (78% ARG, 76% COL), and a medical history of anxiety (31% ARG, 16% COL). Patients in ARG and COL reported a mean(SD) of 15.2 (15.2) and 10.8 (12.1) attacks in the past 6 months, respectively; 60% and 40% of patients, respectively, reported an attack during the past 2 weeks. For 9 (20%) patients in ARG and 1 (4%) patient in COL, the most recent attack affected the throat/larynx. Long-term prophylaxis (LTP) was used by 49% and 56% of patients in ARG and COL, respectively; the most common LTP used in ARG was C1-inhibitor (22%), and in COL were tranexamic acid and danazol (36% each). Mean (SD) AECT scores were 6.04 (2.99) and 7.16 (2.64) in patients in ARG and COL, respectively, indicating their HAE was not controlled. Mean (SD) AE-QoL total scores were 47.12 (23.04) and 50.29 (20.64), respectively, indicating considerable impairment in QoL. HADS and WPAI scores indicated the presence of anxiety, marked impairment in activity, and productivity loss.

Conclusion: The burden of HAE in patients in ARG and COL is substantial. Patients had high attack frequency and impaired health-related QoL. Use of LTP may be limited by the availability of specific treatments in each country.

Conflicts of interest: MW, AS, and DR are full-time employees of Takeda and hold stocks/options. RM and MDLC are full-time employees of ICON, which was contracted by Takeda. RZ reports being a speaker for Takeda, CSL Behring, Novartis, and Sanofi; an advisor for Takeda, CSL Behring, and Abbvie; and a researcher for Takeda and Sanofi. MS was contracted by Takeda to conduct this study.

001071 | Burden of (HAE): Findings from a multinational survey of caregivers for pediatric and adult patients in Argentina and Colombia

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*Presenting author: R. Zwiener

Background: Hereditary angioedema (HAE) is a rare genetic disorder characterised by lifelong recurrent, unpredictable, debilitating swelling attacks that often begin during childhood. There are limited data on the burden for caregivers of pediatric and adult patients with HAE in Latin America.

Method: Two non-interventional, cross-sectional, web-based surveys were conducted with the primary caregivers of (1) pediatric (≤17 years old) and (2) adult patients with HAE (types I/II/normal functioning C1-INH/unknown type) in Argentina (ARG) and Colombia (COL).

Results: In total, 29 caregivers of pediatric patients ($n = 19$ ARG, $n = 10$ COL) and 43 caregivers of adult patients ($n = 29$ ARG, $n = 14$ COL) with HAE participated in the survey. The mean (SD) current age of pediatrics and age at diagnosis was 11.3 (3.9) and 6.5 (4.3) years, respectively, in ARG, and 10.7 (2.6) and 3.2 (2.2) years, respectively, in COL. Mean (SD) duration as caregivers for adults was 15.2 (10.2) and 10.7 (8.4) years in ARG and COL, respectively. In the past 6 months, the mean (SD) attack rate (attacks/month) for pediatrics was 3.67 (3.65) (ARG) and 2.70 (2.00) (COL) and for adults was 15.18 (15.18) (ARG) and 10.84 (12.06) (COL). Pediatrics missed a mean of 4.63 (ARG) and 3.40 (COL) school days in the past 4 weeks due to HAE. Caregivers reported health conditions including migraines, anxiety, and sleeping problems. In the past 4 weeks, caregivers of pediatrics spent a mean of 25.5 (ARG) and 22.1 (COL) days providing care, and missed a mean of 3.3 (ARG) and 1.1 (COL) days of work; caregivers of adults spent 13.4 (ARG) and 16.6 (COL) days providing care and missed 1.1 (ARG) and 2.5 (COL) days of work. For both pediatric and adult patient caregivers, care during the most recent attack commonly involved emotional support, spending time with the patient, helping with medication administration, and advocating for the patient's care; household chores and grocery shopping were also frequently reported by caregivers of adults. Most caregivers reported the emotional impacts of HAE to include worry, sadness, and anxiety.

Conclusion: Frequent HAE attacks were reported for patients in ARG and COL. Caregivers reported a substantial burden associated with caring for patients with HAE, including physical and mental impacts and missed days at work.

Conflicts of interest: MW, AS, and DR are full-time employees of Takeda and hold stocks/options. RM and MDLC are full-time employees of ICON, which was contracted by Takeda. RZ reports being a speaker for Takeda, CSL Behring, Novartis, and Sanofi; an advisor for Takeda, CSL Behring, and Abbvie; and a researcher for Takeda and Sanofi. MS was contracted by Takeda to conduct this study.

001361 | Management of (HAE) with normal C1Inh: About a series of 149 French cases

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*Presenting author: L. Bouillet

Background: Hereditary angioedema with normal C1Inh (HAE-nC1Inh) are very rare diseases. The diagnosis is genetic. The two most frequent mutations are FXII and PLG. The KNG mutation is rarer. Their management is similar to that of AEH with C1Inh deficiency but without evidence based medicine. CREAK has identified all cases of HAE-nC1Inh in order to evaluate their therapeutic management.

Method: This is a national retrospective study conducted in the CREAK network. Each patient identified with an FXII, PLG and KNG mutation was included.

Results: 149 patients were included: 72.5 % with FXII mutation, 27% with the PLG and 1 case with the KNG. 81.4% were women. The average age of the first symptom was 23 years. In 54% of cases, the pill or pregnancy was the revealing factor. 50% of women who have had a pregnancy have seen their disease worsen. At least one laryngeal crisis occurred in 43% of patients. 39% of women received C1Inh concentrate as attack treatment during pregnancy: the treatment was effective and well tolerated in all of them. 27 patients used icatibant for at least one attack: the treatment was effective and well tolerated in all patients. 35 patients required long-term treatment: 62.5% received tranexamic acid, which was effective in 50% of cases; 7 received lanadelumab, fully effective in 83% of the cases; 3 patients improved with berotralstat. For contraception: 27 women were taking a microprogestin pill; 7 an intra uterin advice.

Conclusion: This is an important French series. The evaluation of the management shows that treatments targeting the kallikrein kinin pathway (C1Inh concentrate, ictibant, anti kallikrein) are effective and safe. Of course, this retrospective study needs to be confirmed prospectively.

Conflicts of interest: Takeda, CSL Behring, Biocryst, Novartis, GSK

000711 | The impact of puberty on onset, frequency, location and severity of attacks in (HAE) due to C1-inhibitor deficiency: A survey from the Italian network for hereditary and acquired angioedema (ITACA)

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*Presenting author: R. Senter

Background: Hereditary angioedema due to C1-inhibitor deficiency (HAE-C1INH) is influenced by hormonal factors, with a more severe course of disease in females. Although it has been described that fluctuations in sex hormone can precipitate attacks in HAE-C1INH-patients, no studies had investigated specifically the impact of puberty in these patients. Our study aimed at investigating disease features in HAE-C1INH-patients in accordance with the puberty: disease onset, frequency and sites of attacks, and potential gender differences were addressed.

Method: An observational cohort study has been performed by collecting data through a semi-structured questionnaire from HAE-C1INH-patients referring to 10 Italian Reference Centers in the Italian Network for Hereditary and Acquired Angioedema (ITACA). Inclusion criteria were: (1) a defined HAE-C1INH diagnosis; (2) age between 10 y.o. (if puberty already occurred) and 40 y.o., at the time of the study; (3) inclusion in the ITACA Registry; (4) consent to study. Age of onset of puberty was defined as the age at menarche for females and the age at semenarche for males.

Results: Patients included ($n = 118$) had a F:M ratio 1 and mainly type 1 HAE (95.8%) while type 2 represented rare cases. The median age at the study was 30 years (IQR 13) without a gender difference. The median age at the puberty resulted significantly lower in females (12 yrs, IQR 1.5) than in males (13 years, IQR 2, $p < 0.001$).

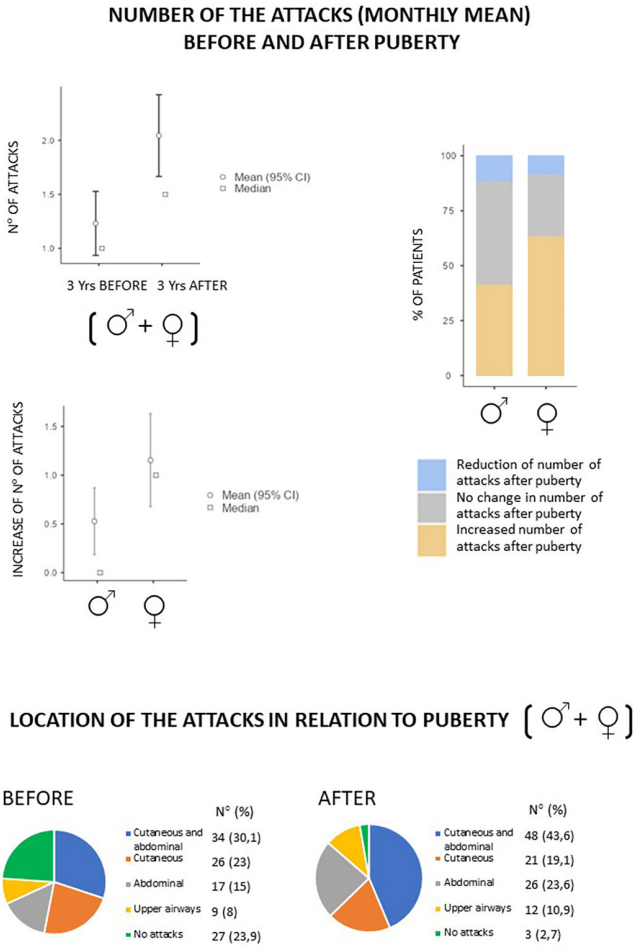
The proportion of symptomatic patients increased significantly after puberty in both males (98.2% vs 83.9%, $p = 0.002$) and females (96.3% vs 68.4%, $p < 0.001$). Among patients ($n = 24$) who became symptomatic after puberty, the first attack occurred after a mean of 5.14 ± SD 4.23 years, without a gender difference.

The median of the monthly number of acute attacks significantly increased after puberty, both in females [3 years before puberty, $n = 0.4$ (IQR 2) vs 3 years after, $n = 2$ (IQR 2.17), $p < 0.001$)] and in males [3 years before puberty, =1 (IQR 1.92) vs 3 years after, $n = 1.25$ (IQR 1.56), $p < 0.001$]. Females showed in a greater proportion than males the increase of attacks (63.2% vs 41.2%, $p = 0.022$); in addition, the amount of increase resulted higher in females [1 (IQR 2)] than in males [0 (IQR1), $p = 0.02$).

No significant differences were detected in the distribution of sites of acute attacks comparing periods before and after puberty, without a gender difference.

In an univariate regression analysis, female gender predicted the worsening of symptoms after puberty (OR 2.44, S.E. 1.65–3.63, $p = 0.02$); the result was similar considering the age of first menstruation as a covariate (OR 2.43, S.E. 1.61–3.68, $p = 0.03$)

Conclusion: Our study documented for the first-time new insights on the impact of puberty on disease features in a large multicenter cohort of HAE-C1INH-patients from the ITACA network, showing that puberty predisposes to increased numbers of angioedema attacks and may be a watershed moment of life when the disease starts to get worse for females.



Conflicts of interest: MC received speaker/consultancy fees from BioCryst, CSL Behring, Kalvista, Pharming, SOBI and Takeda. PT received speaker/consultancy fees from CSL Behring and Takeda FA received consultancy fees or research grants from CSL Behring and Takeda DF received speaking fees or research grants from CSL-Behring and Takeda. MDG received speaker fees from CSL Behring

VM received speaker/consultancy fees from: BioCryst, CSL Behring, GSK, Kyowa Kirin, Takeda, Vifor MG received speaker fees from Takeda, Sanofi and Astrazeneca Other authors have no conflicts of interest to disclose

Flash talks on immune-mediated diseases

100082 | Updated safety and efficacy of NTLA-2002, a CRISPR/Cas9-based gene editing therapy targeting KLKB1, in a Phase 1 study of patients with hereditary angioedema

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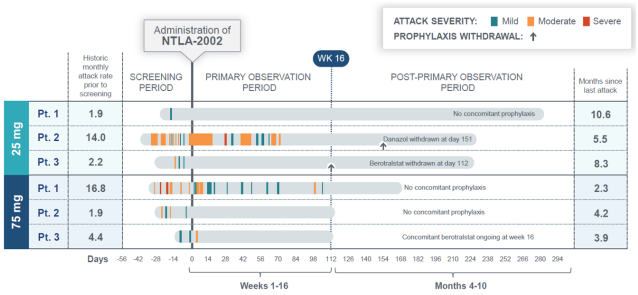
[1]*Amsterdam University Medical Center, Amsterdam, Netherlands*; [2]*Te Whatu Ora, Te Toka Tumai, Auckland, New Zealand*; [3]*Cambridge University Hospitals, NHS Foundation Trust, Cambridge, UK*; [4]*Intellia Therapeutics, Inc, Cambridge, USA*

*Presenting author: R. S. Petersen

Background: Hereditary angioedema (HAE) is a rare, autosomal dominant genetic disease associated with frequent, severe, and unpredictable attacks of swelling due to dysregulated bradykinin production. Treatments targeting kallikrein (encoded by the *KLKB1* gene) significantly reduce attack frequency and improve patient quality of life. NTLA-2002 is an investigational CRISPR/Cas9-based *in vivo* gene editing therapy targeting *KLKB1* in the liver, with the goal of achieving lifelong control of HAE attacks after a single dose. **Method:** A phase 1/2 study of NTLA-2002 in adults with HAE is ongoing, with the phase 1 portion fully enrolled across 3 dosing cohorts: 25mg, $n = 3$; 50mg, $n = 4$; 75mg, $n = 3$. The primary endpoint in phase 1 is safety/tolerability; secondary and exploratory endpoints include pharmacokinetics, pharmacodynamics, and clinical efficacy. Here we present updated safety and efficacy for all 10 patients (pts). **Results:** At the time of interim analysis, median duration of follow-up was 3.8 months (range, 1.0–9.6). Across all dose levels, the most common adverse events (AEs) were infusion-related reactions and fatigue. All treatment-emergent AEs were Grade 1 or 2 only. No clinically significant laboratory findings (including increases in activated partial thromboplastin time), or treatment-emergent serious AEs, were observed. All pts in the 25 mg and 75 mg cohorts completed the 16-week primary observation period and had an ongoing attack-free interval of 2.3–10.6 months (Figure), with a mean reduction in monthly attack rate from weeks 1–16 vs baseline of 91% (25 mg) and 78% (75 mg). For weeks 5–16 vs baseline, the reduction was 89% for both cohorts. Pts who discontinued prophylactic therapy after NTLA-2002 infusion remained attack-free. Steady-state plasma kallikrein protein reduction was observed by in a dose-dependent manner, with mean reductions from baseline of 65%, 81%, and 92% at the 25 mg, 50 mg, and 75 mg doses, respectively. A similar trend in reduction was observed for kallikrein activity. An updated safety and efficacy analysis for all 3 cohorts, including the first analysis of efficacy in the 50mg cohort and 1 year of follow-up for the 25mg cohort, will be presented. **Conclusion:** A single dose of NTLA-2002 was well-tolerated, and led to rapid, robust, dose-dependent, and durable reductions in total plasma kallikrein protein and activity, with clinically significant reduction in attack rate observed in the cohorts analyzed thus far.

Figure. HAE attacks during screening, primary observation, and post-observation period in 25 mg and 75 mg cohorts



HAE attacks during screening, primary observation, and post-observation period in 25 mg and 75 mg cohorts

Conflicts of interest: CB, YX, MCM, AG, JB, MYS, DM: Employees of Intellia Therapeutics and may own stock or stock options. KL, PG, RSP: Nothing to disclose. HL: Acted as a consultant or speaker, received educational sponsorship or participated in research with BioCryst Pharmaceuticals, CSL Behring, Intellia Therapeutics, Ionis Pharmaceuticals, KalVista Pharmaceuticals, Pharming, Pharvaris, Takeda. LMF: Consultancy fee from Pharvaris; travel grant from Ionis Pharmaceuticals. DMC: Speaking fees from CSL Behring, Ionis Pharmaceuticals, Pharvaris, Takeda; consultancy fees from BioCryst, CSL Behring, Ionis Pharmaceuticals, KalVista, Pharming, Pharvaris, Takeda; research support from Ionis Pharmaceuticals, KalVista, Pharvaris, Takeda.

100163 | Api m 10 epitope mapping in a mouse model of honeybee venom sensitization

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*Presenting author: L. G. Fernandes

Background: Evaluation of the molecular sensitization profile of patients by analyzing allergen specific immunoglobulin E (sIgE) plays an important role in the diagnosis of honeybee venom (HBV) allergy. Dominant sensitization to the major allergen Api m 10 has been associated with an increased risk of venom immunotherapy failure in HBV allergy in a retrospective multicenter study, a finding which has been discussed to be related to a lack of instability of Api m 10 in therapeutic venom preparations. To further investigate the role of Api m 10 in the sensitization to HBV, we established a mouse model for HBV and Api m 10 sensitization.

Method: BALB/c mice were sensitized to Api m 10 or to HBV spiked with Api m 10 and evaluated regarding: a) sIgE and sIgG1 response detection by ELISA; b) reactivity of sIgG1 and sIgE to linear epitopes of Api m 10, using 64 synthetic 15-mer peptides with 12 amino acids overlay, spanning the whole amino acid sequence of Api m 10 (isoform variant 1); and c) the basophil activation upon stimulation with HBV, analyzing the frequency and the expression level of CD200R by flow cytometry.

Results: sIgG1 and sIgE to Api m 10 were detected only in mice sensitized with rApi m 10 or HBV spiked with Api m 10, but not in mice that were sensitized just with HBV. sIgE as well as sIgG1 reactivity were detected to two major linear epitopes: peptide number 54, which has been described as the major Api m 10 epitope in humans, and a second peptide number 61. Epitope specific binding was completely abrogated when the serum was previously incubated with rApi m 10. Furthermore, specific activation in basophils from mice sensitized to rApi m 10 or to HBV spiked with rApi m 10 was observed upon stimulation with HBV.

Conclusion: The mouse model of HBV sensitization allowed us to map two major immunodominant linear Api m 10 epitopes for IgE and IgG1. Furthermore, we could demonstrate allergen specific reactivity of basophils from sensitized mice to HBV, suggesting that this model can also be used for functional studies to better understand the role of single allergens in the sensitization and elicitation of HBV allergy.

Conflicts of interest: T. Jakob is or recently was a speaker and/or advisor for and/or has received research funding from ALK-Abello, Allergy Therapeutics/Bencard, Novartis and Thermo-Fisher Scientific.

100498 | Exploring the therapeutic potential of probiotic-derived glyceraldehyde-3-phosphate dehydrogenase (GAPDH) protein as an anti-allergy agent

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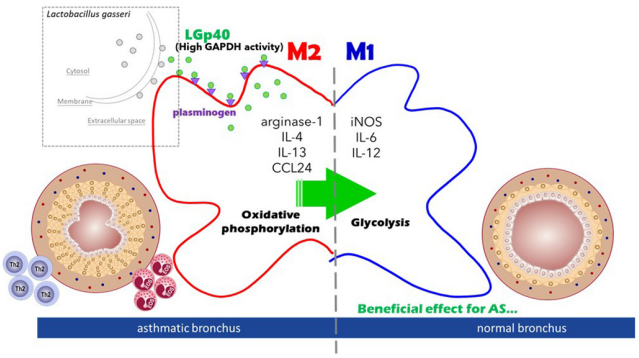
*Presenting author: J. Y. Wang

Background: Probiotic supplementation is emerging as a safe and natural adjuvant treatment for preventing, and/or treatment for allergic diseases. However, clinical probiotic intervention studies have so far yielded contradictory outcomes, which are greatly influenced by host factors. Therefore, it is crucial to investigate the active anti-allergy components of probiotics to dispel uncertainty on whether probiotics will survive and function in recipients.

Method: By extending our previous studies that *Lactobacillus gasseri* inhibits allergic asthma through activating peroxisome proliferator-activated receptor gamma (PPARγ) pathway in dendritic cells and restraining Th2 and Th17 immunity, the anti-allergic inflammation and PPARγ activation component in *L. gasseri* has been identified and purified. Intraperitoneal injection of recombinant component protein was used in a house dust mite (HDM)-induced allergic asthma and atopic dermatitis mouse model to investigate the protective effect.

Results: The anti-allergic ingredient is glyceraldehyde-3-phosphate dehydrogenase (GAPDH) protein, namely LGp40, with multiple intra- and extra-cellular functions beside its glycolytic enzyme activity (moonlighting protein). We confirmed the protection effect of LGp40 in mite-induced allergic asthma and atopic dermatitis mouse models. Both intrarectal inoculation of LGp40-overexpressing *Clear coli* (lipopolysaccharide-free *Escherichia coli*) and intraperitoneal administration of recombinant LGp40 protein attenuated airway allergic inflammation. LGp40 redirected allergic M2 macrophages toward the M1 phenotype and impeded M2-prompted Th2 cell activation through glycolytic activity that induced immunometabolic changes. Recombinant mutant LGp40, without enzyme activity, showed no protective effect against mite-induced airway inflammation. Meanwhile, application of LGp40 in atopic dermatitis-like mice improved the characteristic skin barrier dysfunction and cutaneous type 2 and 17 skewed immunity. LGp40 stopped keratinocyte apoptosis through blocking caspase-3 cascades and activating PPARγ pathway, assisting the maintenance of skin hydration.

Conclusion: Taken together, we found a novel mechanism of moonlighting GAPDH (LGp40) protein that has an important immunoregulatory role in preventing allergic diseases. Our results provide a new strategy for probiotics application in alleviating allergic diseases.



LGP40 induces polarization and functional changes of macrophages.

Conflicts of interest: The authors did not specify any links of interest.

Flash talks on asthma II

100021 | ERS/ATS interpretative strategies for routine lung function tests: Weak agreement between the 2005 and 2021 criteria for bronchodilator response

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*Presenting author: M. Seara Cardoso

Background: Lung function tests (LFT) are important tools in asthma diagnosis and management. In the update of 2021 ERS/ATS interpretive strategies for LFT, a positive bronchodilator response (BDR) was revised as a change of >10% relative to the predicted value in forced expiratory volume in 1st second (FEV_1) or forced vital capacity (FVC). This study aims to explore the differences between the 2005 and 2021 ERS/ATS criteria for BDR applied to patients with asthma.

Method: A retrospective analysis of the patients with a medical diagnosis or suspicion of asthma (≥6 years-old) that performed spirometry from 2014 to 2018 in our lung function laboratory was made. Positive bronchodilator response was evaluated using two different criteria: 2005 ERS/ATS criteria as an increase of ≥12% and ≥200 mL as an absolute value compared with a baseline in either FEV_1 or FVC; and 2021 criteria as a change of >10% relative to the predicted value in FEV_1 or FVC. Agreement analysis between the 2005 and 2021 ERS/ATS criteria for BDR was performed using Cohen's kappa test. The influence of age, ethnic group, predicted FEV_1 and FEV_1/FVC in disagreement between both BDR criteria was analyzed using univariate and multivariate binary logistic regression analyses.

Results: A total of 1078 tests were evaluated including patients from 6 to 88 years old (median: 16; interquartile range: 13) and 50.6% males. According to the 2005 ERS/ATS criteria a positive BDR was found in 43.6% of patients and using the 2021 criteria 27.6% had a positive BDR. Cohen´s kappa for agreement between both criteria was 0.595 ($p < 0.0001$). The univariate analysis showed significant associations of disagreement between both BDR criteria and male gender [odds-ratio (OR) 1.74, $p < 0.0001$], height (cm, OR 1.04, $p < 0.0001$), predicted FEV_1 (L, OR 2.09, $p < 0.0001$) and FEV_1/FVC (OR 0.05, $p < 0.0001$). The multivariate logistic regression analysis showed a significant association between predicted FEV_1 (L, OR 1.96, $p < 0.01$) and FEV_1/FVC (OR 0.09, $p < 0.01$) and disagreement between both BDR criteria.

Conclusion: In our study, there was a weak agreement between the 2005 and 2021 ERS/ATS criteria for positive bronchodilator response. The odds of disagreement between both criteria were superior in patients with higher predictive FEV_1 and lower with higher FEV_1/FVC. Further studies should be made to assess the clinical impact of the 2021 ERS/ATS update for BDR criteria.

Conflicts of interest: The authors did not specify any links of interest.

100031 | Molecular sensitisation profile to dogs in residents of latvia and its connection with asthma and the course of allergic rhinitis

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Background: Studies show that the prevalence of sensitisation to dog allergens is increasing, and this sensitisation is associated with increased asthma development risk.

The aim of our study was to evaluate the dog allergen molecular sensitisation profile, its connection to the presence and control of asthma and the severity of allergic rhinitis in patients living in Latvia.

Method: This was a retrospective, observational, cross-sectional study. In dog-sensitized patients in whom ELISA-based in-vitro multiplex Allergy Explorer (ALEX, MADX) test was performed, data about age, gender, presence or absence of diagnosis of asthma, and sensitisation to dog allergen molecules (Can f 1, Can f 2, Can f 3, Can f 4, Can f 5 and Can f 6) were collected. Additional data were collected about asthma control status according to Global Initiative for Asthma (GINA) criteria. The odds ratio of asthma presence, asthma control, and course of allergic rhinitis in patients with positive vs negative dog allergen component-specific IgE were calculated using Chi-square or Fisher's exact test. The study was approved by the Ethics committee of the University of Latvia.

Results: 91 (29.3%) of all 311 ALEX-tested patients were sensitised to dogs. 18 (9.8%) patients were monosensitised to dogs. 81 (87.9%) of patients were diagnosed with allergic rhinitis, but 53 (58.2%) – had a diagnosis of asthma. 63.7% of patients were sensitised to Can f 1 molecule, 62.0% to Can f 5, 36.6% to Can f 6, 21.1% to Can f 4, 16.5% to Can f 2 and 15.4% to Can f 3. Sensitisation to Can f 1 was associated with 3.41 times higher ($p = 0.006$), to Can f 2 with 5.85 times higher ($p = 0.020$) and to Can f 6 with 4.17 times higher ($p = 0.008$) asthma risk. In 18 dog monosensitised patients, higher asthma risk was found only with positive specific IgE to Can f 1 and Can f 2, by 3.32 ($p = 0,011$) and 12.77 ($p = 0.004$) times higher, respectively. A higher count of positive specific IgE to various dog allergen molecules was associated with increased asthma risk ($p = 0.006$). No correlation was found between sensitisation profile, positive sensitisation count and asthma control status. Dog allergy component IgE for Can f 1 and Can f 3 had a statistically significant impact on the severity of allergic rhinitis.

Conclusion: Sensitisation count and specific sensitisation to dog allergen molecules, Can f 1, Can f 2 and Can f 6, may impact asthma risk. Sensitisation to Can f 1 and Can f 3 may be associated with a more severe and persistent course of allergic rhinitis.

Conflicts of interest: The authors did not specify any links of interest.

100117 | Obese and non-obese patients with severe asthma: Comparison of omalizumab-mepolizumab treatment outcomes

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Background: In obese severe asthmatics, the degree of type 2 inflammation may vary according to their atopic status and past smoking history. In this study, we aimed to analyze the clinical and physiopathological features of obese and non-obese severe asthmatics treated with omalizumab or mepolizumab treatment. In addition we aimed to compare the clinical, spirometric outcomes and total peripheral eosinophilic count (TEC) changes after treatment with these two biologic agents in obese and non-obese groups.

Method: In this retrospective, cross sectional study, 180 adult patients with severe asthma from 3 centers were evaluated. Of these patients, 59 patients were excluded due to missing data; 121 were treated with biologic agents (omalizumab = 88 or mepolizumab = 33) for at least 16 weeks were included in the study. Obese (*n*: 44) and non-obese severe asthmatics (*n*: 77) were analyzed according to whether they provided a heavy smoking history (≥10 packs/year) and were found to be atopic. Obese and non-obese groups were compared in terms of the change in the asthma control test (ACT), asthma attacks, TEC and FEV_1 after treatment

Results: In patients with a heavy smoking history, non-obese group had a significantly higher TEC compared to obese group ($p = 0.013$) (Table 1). Within the non-obese group, non-atopic patients had a significantly higher TEC compared to atopic patients ($p = 0.021$) (Table 2). Both biologic agents had similar effects on improving ACT and in reducing asthma attacks; however, mepolizumab was more effective in suppressing TEC. The improvement in FEV_1 in obese group following biologic two agents was very similar but in non-obese group, mepolizumab was found to be superior.

Conclusion: In our real-life study, non-obese severe asthmatics with a history of heavy smoking and those that were non-atopic had higher TEC. Compared to omalizumab, mepolizumab was superior at reducing TEC in all asthmatics and in improving FEV_1 in non-obese group.

Table 1:Analysis of Patients According to Heavy Smoking History

	OBESE ASTHMATICS			NON OBESE ASTHMATICS		
	Heavy Smoker n:10	Light Smoker n:34	p value	Heavy Smoker n:10	Light Smoker n:34	p value
TEC (cells/µl), Median (Min.-Max.)	300.00 (100-770)	400.00 (0-2800)	0.121*	660.00+ (200-1500)	400.00 (0-2730)	0.279*
FEV_1(ml), Mean±SD	1727.50±435.52	1846.88±626.17	0.620**	2012.22±1010.60	1907.23±701.41	0.704**
$FEF_{25-75\%}$, Mean±SD	53.00±25.51	52.78±22.06	0.982**	46.25±23.25	51.64±23.36	0.558**
Asthma Attack, Median (Min.-Max.)	6.00 (3-20)	5.00 (2-15)	0.534*	6.00 (3-12)	6.00 (1-20)	0.990*

*:Mann Whitney U Test

**:Independent Sample T test

+:When obese and nonobese patients were analyzed according to their exposure to heavy smoking history, the baseline eosinophil level of patients with a heavy smoking history in the nonobese group was significantly higher than in the obese group.[Median:660 (Min:200-Max:1500)vs Median:300(Min:110-Max:770) ;p=0.013,Mann Whitney U Test]

Abbreviations: TEC:Total peripheral eosinophil count

Acronyms: Heavy Smoker:≥10 Pack- year Smoking History, Light Smoker:<10 Pack-year Smoking History

Conflicts of interest: The authors did not specify any links of interest.

100121 | Is airway variability increased in patients with a history of NSAID hypersensitivity?

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are the drugs that cause the most common drug hypersensitivity reactions (HSR) all over the world. According to the current classification, EAACI/ENDA and GA2 LEN/HANNA, NSAID-associated HSR has also been defined as "immunological" and "non-immunological" according to the underlying mechanism. Reactions to more than one NSAID whose non-immunological HSRs are chemically dissimilar, but whose common feature is to inhibit the pharmacological COX-1 enzyme, occur early and are referred to as "cross-reaction" type NSAID sensitivity. In clinical practice, we observed that especially patients with a history of cross-reactive NSAID HSR have higher airway reversibility, and starting from this, we aimed to compare the FEV1 changes of patients with a history of NSAID HCR after salbutamol with a healthy control group.

Method: The data of patients who came to our clinic with a history of NSAID HSR were analyzed retrospectively, and patients with NSAID-exacerbated cutaneous disease (NECD) were excluded from the study. Patients with underlying asthma (NERD) in the cross-reactive group were defined as - NSAID-triggered Urticaria/Angioedema (NIUA), Single NSAID-triggered Urticaria/Angioedema or Anaphylaxis (SNIUAA). PFT records of the control group without smoking history and underlying lung disease were obtained from the general examination outpatient clinic. The files of 92 patients with a history of NSAID HCR were evaluated retrospectively. 29 patients whose PFT could not be reached were excluded. Spirometric

measurement values and post-bronchodilator reversibility levels were compared between these 4 groups.

Results: Of the 92 patients with a mean age of 39.52 ± 13.53, .80 women, 19 were NERD, 17 were NIUA, 27 were SNIUAA. 28 patients were in the control group (Table 1). When the PFT values were compared, as seen in Table 1, the basal FEV1 levels of the groups were similar, while the FEV1 change after salbutamol was higher in favor of the cross-reactive group.

Conclusion: Airway variability is affected rather than baseline FEV1 in patients with a history of NSAID HCR, and FEV1 change tends to increase after salbutamol, especially in the presence of cross-reactivity, and these patients should be followed up for the development of asthma.

	NERD	NIUA	SNİUAA	Control Group	p value
Basal FEV_1, mean±SD	1610.28±961.06	2910,00±819.00	2800.00±890.00	2800.71±827.12	0.289*
FEV_1 change, mean±SD	258.00±139.50	231.43±252.95	136.00±170.40	62.86±129.13	0.002*
*:One way ANOVA test					

Table 1

Conflicts of interest: The authors did not specify any links of interest.

100133 | Understanding the effect of clinical baseline characteristics on SABA reliever use in patients with moderate-severe asthma

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*Presenting author: I. Pavord

Background: Factors driving short-acting β-agonist (SABA) use are not fully characterised in patients with moderate-severe asthma. There is limited insight on the effect of exacerbations on reliever medication use. Using data from adult patients enrolled in clinical trials, we previously developed a Poisson model to describe individual patterns of SABA use during regular dosing with fluticasone propionate (FP) monotherapy, or combination therapy with FP/salmeterol (FP/SAL) or budesonide/formoterol (BUD/FOR). Time since asthma diagnosis, symptom control level (ACQ-5), body mass index and smoking status at baseline correlated strongly with SABA use irrespective of treatment. Here we present results of the initial exploratory phase to assess the influence of exacerbations on SABA reliever use and the effect of symptom control levels.

Method: Baseline characteristics and daily SABA use data (overnight uses and past 24h puffs) from adult patients with moderate or severe asthma ($n = 5554$) were aggregated from a patient pool ($N = 16,232$). Graphical analysis was used to support covariate selection during model development and explore the long-term effect of exacerbations on SABA reliever use. Observed and predicted patterns of SABA use were derived using final parameter estimates from the Poisson model. SABA count data were summarised graphically, stratified by treatment and exacerbation status. Variation in SABA counts in the overall population was compared with those with poor symptom control at baseline.

Results: SABA use decreased over 12 months with the steepest decline occurring in the initial phase. This effect was most prominent in patients with average >1–2 puffs per day. SABA use was consistently higher in patients with ≥1 exacerbation compared with patients without exacerbations, particularly in patients with baseline ACQ-5 ≥1.5. Accounting for covariate effects, clinically relevant differences in SABA use were seen in patients receiving FP monotherapy vs FP/SAL or BUD/FOR. An overview of SABA use by treatment and exacerbation status is presented (Figure 1).

Conclusion: SABA use is higher in patients who exacerbate. This effect persists over the course of treatment and appears to be more evident in those with poor symptom control receiving regular ICS or ICS/LABA. Changes in SABA use patterns together with

other baseline patient characteristics could be used as a measure of asthma control in clinical settings where ACQ-5 scores are not regularly assessed.

Funding: GSK (study ID 215310)

Figure 1: Observed SABA use (overnight occasions and past 24h SABA puffs) in patients with moderate-severe asthma

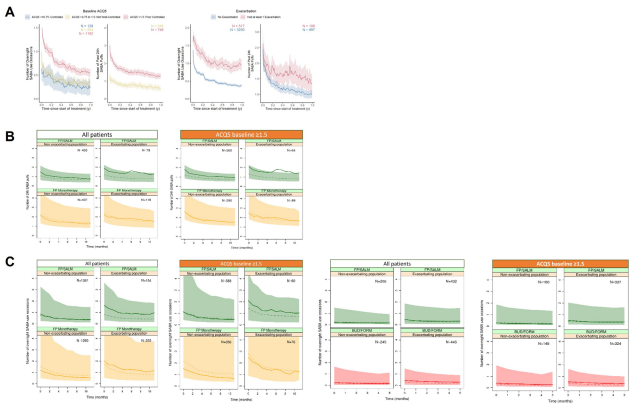

Figure legend (Results):

(A) Observed SABA use (24h puffs and overnight occasions) over time in the overall population, stratified by symptom control level at baseline (ACQ-5) (left) and by occurrence of exacerbations (right). **(B)** Mean SABA use (24h puffs) over time, stratified by treatment group and occurrence of exacerbations in the overall study population (**left**) and in patients who show poor symptom control at baseline (ACQ-5 ≥1.5) (right). **(C)** Mean SABA use (overnight uses) over time in the overall study population (left) and in patients who show poor symptom control at baseline (ACQ-5 ≥1.5) (right), stratified by treatment group and occurrence of exacerbations. In addition to the effect of time since asthma diagnosis, symptom control level (ACQ-5), body mass index and smoking status at baseline, it is important to note the impact of study duration and inclusion/exclusion criteria on the overall pattern of SABA use when comparing treatment response. Solid and dashed lines represent the observed and model-predicted profiles, respectively. Shaded area depicts the 90% prediction interval. N indicates the number of patients in each group.

Mean patterns describe both exacerbating and non-exacerbating patients, with exacerbation defined as in the original study protocols: use of systemic corticosteroids for ≥3 days, OR in-patient hospitalisation, OR emergency department visit due to asthma requiring systemic corticosteroids. The doses used in the simulations were based on individual response and/or protocol asthma control plan (FP: 100, 250 and 500 mcg twice daily;
FP/SAL: 100/50, 250/50 and 500/50 mcg twice daily; BUD/FOR: 160/4.5 and 320/9.0 mcg twice daily). Text in each panel indicates the number of patients in each category or group.

Abbreviations: ACQ-5, Asthma Control Questionnaire 5; BUD, budesonide; FOR, formoterol; FP, fluticasone propionate; ICS, inhaled corticosteroid;
LABA, long-acting β_2-agonist; SABA, short-acting β_2-agonist; SAL, salmeterol

Conflicts of interest: IP has received honoraria for speaking at sponsored meetings from AstraZeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, Teva, Chiesi, Sanofi/Regeneron, Menarini and GSK, and payments for organising educational events from AstraZeneca, GSK, Sanofi/Regeneron and Teva; he has received honoraria for attending advisory panels with Genentech, Sanofi/Regeneron, AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Teva, Merck, Circassia, Chiesi and Knopp and payments to support FDA approval meetings from GSK; he has received sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, AstraZeneca, Teva and Chiesi; he has received a grant from Chiesi to support a Phase 2 clinical trial in Oxford; he is co-patent holder of the rights to the Leicester Cough Questionnaire and has received payments for its use in clinical trials from Merck, Bayer and Insmed; and in 2014–2015 he was an expert witness for a patent dispute involving AstraZeneca and Teva; DS has received personal fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Epiendo, Genentech, GSK, Glenmark, Gossamerbio, Kinaset, Menarini, Novartis, Pulmatrix, Sanofi, Synairgen, Teva, Theravance and Verona; GG has participated in advisory boards for GSK, AstraZeneca, Sanofi, Novartis and Boehringer Ingelheim; he has received honoraria for speaking at sponsored meetings from GSK, Boehringer Ingelheim, AstraZeneca, Sanofi, Phoenix and Novartis; and is a principal investigator in trials sponsored by GSK, Boehringer Ingelheim, AstraZeneca, Novartis, Sanofi, PPD, Zambon, Parexel, Covance, IQVIA and Chiesi; APG, CT, ODP, SO and SCvD are GSK employees and hold stocks/shares in GSK. Editorial support was provided by Katy Widnall of Fishawack Indicia Ltd, UK, part of Fishawack Health.

100170 | The non-interventional real-life study with a combination of beclomethasone dipropionate and formoterol in HFA or DPI 100/6 µg inhalers as maintenance and reliever therapy in patients with moderate persistent uncontrolled asthma

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Background: Several international guidelines recommend using ICS/formoterol as a maintenance treatment and as-needed reliever therapy (MART). The MART strategy using the combination of BDP/F has been studied in several clinical trials in patients with moderate asthma and significantly reduced asthma exacerbation rate. The aim of the study was to evaluate the efficacy of BDP/F MART in a real-life study in patients with moderate, persistent, uncontrolled asthma previously treated with continuous maintenance therapy and short-acting β2-agonists (SABA) per need.

Method: This was a 24-week, prospective, multicenter, open-label, non-interventional study in 6 research centres in Latvia. Patients were treated with beclomethasone/formoterol 100/6 µg HFA pMDI or DPI inhaler 1 – 2 inhalations twice daily and as needed up to a maximum of 8 inhalations per day. Data about asthma control status (well controlled, partially controlled, uncontrolled) according to Global Initiative for Asthma (GINA) recommendations, lung function, symptom score and patient satisfaction (SatQ questionnaire) were collected at baseline and week 4, 12 and 24. The Ethics committee of the University of Latvia approved the study protocol.

Results: 61 patient was recruited in our study, and 52 patients arrived to visit 4 at week 24. The mean age of the recruited patients was 54.9 (95% CI 51.3; 58.5) years. 41 (67.2%) were females. The average height was 1.68 (95% CI 1.66; 1.70) m, BMI – 30.7 (95% CI 28.9; 32.5) kg/m2, asthma history - 10.4 (95% CI 7.5; 13.4) years, and mean FEV1 at baseline - 88.4% (95% CI 84.1; 92.7%). 39 (63.9%) participants were non-smokers, 18 (29.5%) – were ex-smokers, and 4 (6.6%) - were smokers. Study treatment provided a significant shift of asthma control status from an uncontrolled to a partially controlled or well-controlled state at weeks 4, 12 and 24 ($p < 0.001$). We observed significant improvement of FEV1 by 100 to 160 ml ($p < 0.05$) and a reduction of average symptom score from 1.5 to 0.5 (score 0–3) vs baseline at weeks 4, 12 and 24 ($p < 0.0001$). At week 12, 17% of patients were very satisfied, 44% were satisfied, and 8%

were neutral about the study treatment. At week 24, 28% were very satisfied, 40% were satisfied, 8% neutral, and 3% were unsatisfied.

Conclusion: Study treatment provided substantial improvement in asthma control status and lung function. Most patients were satisfied with the study treatment and got a significant reduction in asthma symptom scores.

Conflicts of interest: The study was sponsored by the closed JSCo Norameda and Chiesi Farmaceutici S.p.A

100427 | Dysregulation of matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) leads to lung fibrosis in house dust mite-induced experimental asthma

A. Janucik[1]; M. Tynecka[1]; A. Tarasik[1]; B. Hanczaruk[1]; A. Walewska[1]; A. Zbikowski[1]; M. Niemira[1]; J. Zebrowska[1]; A. Szalkowska[1]; U. Korotko[1]; J. Reszec[1]; A. Kulczynska-Przybik[1]; M. Kwasniewski[1]; B. Mroczko[1]; A. Kretowski[1]; M. Sokolowska[2]; C. Karaaslan[3]; M. Moniuszko[1]; A. Eljaszewicz[1]

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Background: Matrix metalloproteinases (MMPs) are enzymes playing a key role in extracellular matrix remodeling in the course of tissue repair and inflammation. MMPs regulate the breakdown and turnover of extracellular matrix (ECM) components. Their activity is tightly controlled by tissue inhibitors of matrix metalloproteinases (TIMPs). The balance between MMPs and TIMPs is critical for proper lung regeneration, and disruption in their activity and function may lead to lung fibrosis. Here we aimed to investigate the role of MMPs and TIMPs in house dust mite-induced experimental asthma.

Method: Acute (2 weeks) and chronic (12 weeks) airway inflammation was induced by intranasal administration of 10 mg or 100 mg house dust mite extract (HDM) to C57BL/6J mice. Lung tissue was collected for gene expression analyses, histological staining, flow cytometry, and targeted protein analyses.

Results: First, we confirmed increased immune cell infiltration in total collagen deposition in the lungs after HDM administration. We observed an elevated frequency of IL-4 and IL-17-producing T cells. Transcriptomic analyses revelated dysregulated expression of genes related to ECM morphology, collagens, MMPs, and TIMPs. Proteomic profiling of bronchoalveolar lavage revealed increased levels of MMP-2 and TIMP-4 in all investigated models, whereas MMP-8 was uniquely elevated in the chronic model. Immunohistochemical staining showed increased deposition of Collagen I, III, and VI in both models.

Conclusion: Taking together, we showed a disrupted balance between MMPs and TIMPs, which may contribute to increased collagen deposition and pathological ECM reconstruction leading to airway fibrosis.

Conflicts of interest: This study is supported by a grant from the National Centre for Research and Development (POLTUR3/MT-REMOD/2/2019). Adrian Janucik, Bartosz Hanczaruk and Arkadiusz Żbikowski are supported by the program "Best of the Best 4.0 (original name: Najlepsi z Najlepszych 4.0)" founded by the Ministry of Education and Science.

100429 | The influence of adipose tissue-derived mesenchymal stem cells (MSC) administration in the house dust mite (HDM-induced) mixed airway inflammation model

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Background: The immunosuppressive properties of MSCs have been successfully evaluated in numerous preclinical, experimental asthma models mirroring Th2-driven (eosinophilic) asthma. However, their effects on mixed airway inflammation combining the involvement of Th2 and Th1/17 related responses, remain elusive. Therefore, here we aimed to investigate the effects of MSC intranasal administration on mixed airway inflammation in the HDM-induced experimental asthma model.

Method: Female C57BL/6J mice were treated intranasally with 10 mg of HDM extract for five days, following two days without stimulation, in a two-week cycle. MSC were administrated intranasally at days 6 and 13 of the experiment to investigate long- and short-term effects, respectively. All animals were sacrificed on the 15th day. To assess immune cell infiltration and mucus production, lungs were collected for histochemical staining. In addition, T-cell effectors were analyzed using flow cytometry. Furthermore, epithelial barrier integrity was assessed by using fluorescence staining. Finally, RNA was isolated from the lung specimens, and transcriptomic profiling was performed using the Illumina platform.

Results: First, we observed that intranasal MSC administration significantly limits mixed airway inflammation. We found the significant limitation of inflammatory cell infiltration within the lung, decreased mucus production, and decreased frequency of INFg and IL-17-producing T cells after MSC administration. Next, we assessed epithelial barrier integrity and observed increased ZO-1 expression. Finally, the analysis of signaling pathways and biological functions showed decreased expression of genes related to immune responses, including mast cell migration and B cell receptor immune responses, leukocyte migration, and recruitment of neutrophils and eosinophils.

Conclusion: In summary, we confirmed that administration of adipose tissue-derived MSC limits airway inflammation in the mixed inflammation experimental asthma.

Conflicts of interest: Bartosz Hanczaruk, Arkadiusz Zbikowski, and Adrian Janucik are supported by the program "Best of the Best 4.0

(original name: Najlepsi z Najlepszych 4.0)" founded by the Ministry of Education and Science.

100431 | The influence of intranasal adipose tissue-derived mesenchymal stem cells (MSCs) administration on noninflamed lung in mice

A. Żbikowski[1]; A. Janucik[1]; M. Tynecka[1]; B. Hanczaruk[1]; A. Tarasik[1]; M. Niemira[1]; A. Walewska[1]; J. Zebrowska[1]; A. Szalkowska[1]; U. Korotko[1]; J. Reszec[1]; M. Kwasniewski[1]; A. Kretowski[1]; M. Sokolowska[2]; M. Moniuszko[1]; A. Eljaszewicz[1]

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*Presenting author: A. Żbikowski

Background: The immunoregulatory properties of mesenchymal stem cells (MSCs) have been successfully tested in numerous preclinical studies, including asthma models. Despite significant progress in the understanding of mechanisms underlying MSC-mediated suppression of chronic inflammation in respiratory diseases, the implementation of MSC-based therapy in clinical routine still meets many concerns regarding safety and stability. Here we aimed to assess the influence of intranasal (i.n.) adipose tissue-derived MSCs administration to the noninflamed lung in an experimental mice model.

Method: To assess short- and long-term effects of intranasal adipose tissue-derived MSCs administration, C57BL/6 mice were sacrificed after 2 and 9 days from cell transfer, respectively. The lungs were collected for histochemical staining's transcriptomic profiling, flow cytometry, and confocal microscopy.

Results: We did not observe inflammatory infiltration or mucus overproduction within the lung tissue after MSC application. Surprisingly, however, we found a significantly increased frequency of IFNg-producing T helper cells and decreased expression of Claudin 3 and Occludin as a long-term effect of MSCs administration. Transcriptomic profiling revealed dysregulation of genes related to redox imbalance and hypoxia signaling pathways. We observed changes in genes clustered in the pattern recognition receptors, macrophage activation, oxidative stress, and phagocytosis.

Conclusion: In summary, our results indicate that intranasally administrated MSC undergoes apoptosis in a non-inflammatory lung leading to low-grade inflammation and barrier opening top clear the graft.

Conflicts of interest: This study is supported by a grant from the National Centre for Research and Development (POLTUR3/MT-REMOD/2/2019). Adrian Janucik, Bartosz Hanczaruk and Arkadiusz Żbikowski are supported by the program "Best of the Best 4.0 (original name: Najlepsi z Najlepszych 4.0)" founded by the Ministry of Education and Science.

Flash talks on food allergy and immunotherapy

100515 | An innovative approach & risk factors for stratifying risk for pediatric food allergies

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*Presenting author: T. Landau

Background: There currently is no clinical standard of care for stratifying one's chances of developing food allergies, despite numerous studies pointing to genetic, environmental and medical history risk factors for the conditions. A family history of atopic conditions has been used to identify high-risk infants in the research setting yet fails to distinguish between genetic and environmental risk factors. We aimed to characterize risk factors that are derived from well-known epidemiological studies to harness the data available in electronic medical records to stratify risk for food allergies.

Method: We performed a retrospective, cross-sectional database study on the Leumit Health Services electronic medical record database (Israel). Infant-mother dyads were included if the infant was born after 2010 and was diagnosed with food allergy by an allergist before reaching four years of age ($n = 4{,}077$) and were compared with a cohort of non-food allergic children ($n = 95{,}686$). Raw clinical variables include parental, sibling and infant history of atopic conditions, gender, season of birth, maternal medications while pregnant, and previous diagnoses. All variables were derived from the prenatal and postnatal period prior to the food allergy diagnosis, but no later than from 6 months of age. Logistic regression and machine learning predictive models were trained and tested on the combined dataset.

Results: Significant risk factors include use of systemic antibiotics during pregnancy (OR 2.08, CI 2.00–2.15, $p < 0.001$), percent of siblings with an atopic condition (OR 1.93, CI 1.72–2.16, $p < 0.001$), a known parental atopic condition (OR 1.28, CI 1.23–1.34, $p < 0.001$) and a prior diagnosis of atopic dermatitis (OR 9.78, CI 8.98–10.65, $p < 0.001$). Receiver operating characteristic curve analyses showed an area under the curve of 0.8 for a random forest regressor. The model boasts accuracy of 86%, with corresponding sensitivity of 58%, and specificity of 87%.

Conclusion: Atopic history of the infant and sibling history of atopic conditions reflect the confluence of both genetic and environmental factors, and both prove to be important and easily accessible variables that can be used in the clinical or research setting. Additional variables including parental history of atopic conditions and maternal antibiotic use contribute towards an infant's risk of developing food allergies. Taken together, these easy-accessible variables allow predictive modeling using routinely collected electronic medical record data to stratify an infant's risk of developing food allergy.

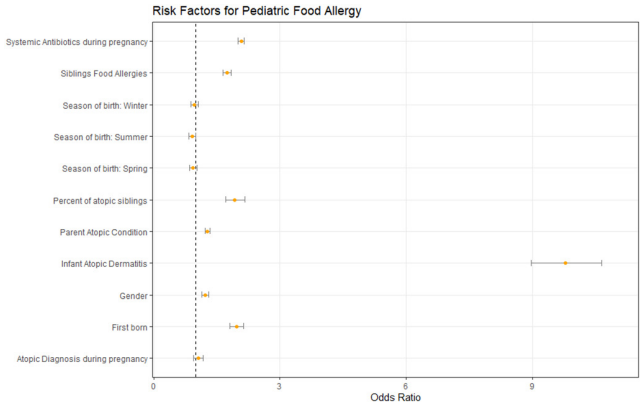

Figure 1. Odds ratios and confidence intervals for variables in logistic regression model to stratify risk for pediatric food allergy. All variables are significant (p-value < 0.001) other than season of birth and atopic diagnosis during pregnancy.

Conflicts of interest: The authors did not specify any links of interest.

100047 | **Short-term benefits of sublingual allergen immunotherapy in routine clinical practice: Observed disease evolution in the observational, prospective, longitudinal study practis**

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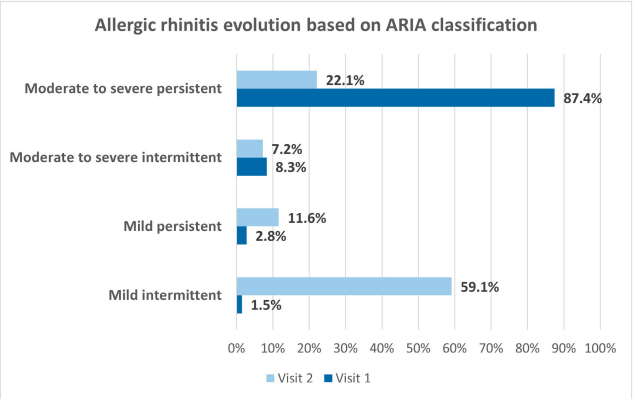
*Presenting author: J. Cottet

Background: Allergen immunotherapy (AIT) is a typical model of precision and personalised medicine which can be adapted to the patient clinical and sensitisation profile. The PRACTIS study conducted among allergy specialists in France aimed at evaluating in current practice the short-term benefits of sublingual allergen immunotherapy (SLIT) after 6 to 12 months in patients with allergic rhinitis (AR) ± asthma (AA) ± conjunctivitis (AC) according to the modalities of use. Here, we present the evolution of AR, AA and AC symptoms and rescue medication (RM) use overtime in treated patients.

Method: In this prospective, non-interventional, longitudinal, multicentre study, AIT-eligible patients (age ≥5 years) with medically confirmed allergy to one or more allergens were evaluated at inclusion prior to SLIT initiation (Visit 1) and after 6 to 12 months of treatment (Visit 2). Physicians collected patient data in a CRF including the symptom evolution and use of RM for AR, AA and AC between the start and end of study. Disease evolution was compared in subgroups by age category, SLIT formulation and type of allergens.

Results: A total of 1587 evaluable patients (adults 60.4%, adolescents 14.4%, children 25.2%) received SLIT liquid (71.8%) or tablets (28.2%) of allergen extracts, more frequently house dust mites (51.2%), grasses (28.7%), trees/weeds (15.1%), animal danders (2.7%) and moulds (1.0%). At end of study, in the 1047 patients who attended Visit 2, overall symptom improvement was achieved in 80.3% (823/1025) patients with AR, 68.0% (217/319) with AA and 77.5% (437/564) with AC. Consistent results were observed regardless of age category, SLIT formulation and type of allergens except for a significantly more important impact on AA in pollen allergic patients (Table). Based on ARIA classification, AR symptom frequency and severity shifted from persistent (~90% of patients at Visit 1) to intermittent and from moderate-to-severe (~96% of patients at Visit 1) to mild for about 2/3 of patients at Visit 2 (Figure). In addition, a decrease or no RM use was seen in about 7/10 patients with AR and/or AA and 8/10 patients with AC, regardless of their age.

Conclusion: In current practice, treatment with SLIT demonstrated short-term benefits in patients with AR/AA/AC in terms of symptom improvement and medication use mostly regardless of their age, the SLIT formulation and the type of causal allergen.



Age groups											
		Children (5-11 y)		Adolescents (12-17 y)		Adults (≥18 y)		Population who completed V2		p value	
AR	n	273		146		606		1025			
	Symptom improvement		81.7%		77.4%		80.4%		80.3%	0.390	[b]
	n	273		146		605		1024			
	No RM use		24.9%		28.1%		23.6%		24.6%	0.735	[b]
	Decrease in RM use		44.7%		46.6%		49.8%		47.9%		
AA	n*	139		39		141		319			
	Symptom improvement		69.1%		69.2%		66.7%		68.0%	0.697	[b]
	n	150		44		177		371			
	No RM use		30.7%		50.0%		44.6%		39.6%	0.078	[b]
	Decrease in RM use		33.3%		15.9%		26.0%		27.8%		
AC	n*	125		73		366		564			
	Symptom improvement		80.8%		75.3%		76.8%		77.5%	0.516	[b]
	n	159		96		432		687			
	No RM use		50.9%		56.3%		47.0%		49.2%	0.730	[b]
	Decrease in RM use		30.8%		26.0%		33.8%		32.0%		

Type of formulation							
		Tablet		Liquid		Population who completed V2	p value
AR	n	309		717		1026	
	Symptom improvement		82.2%		79.5%	80.3%	0.576 [b]
	n	309		716		1025	
	No RM use		28.5%		22.9%	24.6%	0.114 [a]
	Decrease in RM use		48.5%		47.8%	48.0%	
AA	n*	77		242		319	
	Symptom improvement		70.1%		67.4%	68.0%	0.918 [b]
	n	94		277		371	
	No RM use		50.0%		36.1%	39.6%	0.083 [b]
	Decrease in RM use		24.5%		28.9%	27.8%	
AC	n*	192		373		565	
	Symptom improvement		81.8%		75.3%	77.5%	0.211 [b]
	n	226		462		688	
	Decrease in RM use		49.6%		48.9%	49.1%	0.189 [b]
	No RM use		35.4%		30.5%	32.1%	

Type of allergen								
		House dust mites	Grasses	Trees/Weeds	Animal danders	Moulds	Population who completed V2	p value
AR	n	501	322	146	28	8	1005	
	Symptom improvement	80.4%	82.3%	80.1%	67.9%	62.5%	80.5%	0.242 [b]
	n	501	322	145	28	8	1004	
	No RM use	27.5%	22.4%	21.4%	21.4%	12.5%	24.7%	ND
	Decrease in RM use	45.3%	53.1%	49.0%	39.3%	37.5%	48.1%	
AA	n*	188	81	27	11	4	311	
	Symptom improvement	63.8%	77.8%	85.2%	45.5%	50.0%	68.5%	**0.016** [b]
	n	212	97	36	13	4	362	
	No RM use	34.9%	47.4%	55.6%	23.1%	25.0%	39.8%	**0.053** [b]
	Decrease in RM use	27.8%	30.9%	19.4%	15.4%	50.0%	27.6%	
AC	n*	171	246	114	14	5	550	
	Symptom improvement	78.9%	79.7%	75.4%	64.3%	40.0%	77.8%	0.066 [b]
	n	253	273	123	16	6	671	
	Decrease in RM use	62.1%	44.3%	34.1%	62.5%	33.3%	49.5%	ND
	No RM use	23.3%	38.1%	40.7%	12.5%	16.7%	32.2%	

AA: Allergic asthma, AC: Allergic conjunctivitis, AR: Allergic rhinitis, N: Number of patients, n: Number of patients with data, n: Number of patients presenting with the disease and for whom physicians considered the question applicable, NA: Not Available (Test result not available due to memory problems), ND: Not Determined, RM: Rescue Medication; [a] Chi² test, [b] Fisher's exact test*

Conflicts of interest: H Nguyen is an employee of Stallergenes GreerS Scurati is an employee of Stallergenes GreerP Demoly reports having received honorarias for teaching, research and humanitarian activities from: ALK-Abelló, AstraZeneca, GlaxoSmithKline, Menarini, Puressentiel, Stallergenes Greer, ThermoFisher Scientific, Viatris, ZambonH Chabane reports having received fees for participation in congresses and/or advisory boards from ALK-Abelló, Glaxo Smith Kline, Stallergenes Greer and ThermoFisher Diagnostics

100058 | An accelerated up-dosing scheme using one strength for SCIT with a native HDM allergen extract proved safety and tolerability in Chinese children with allergic rhinitis with or without asthma

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*Presenting author: J. Bai

Background: The poor long-term adherence is known to affect the efficacy of allergen immunotherapy (AIT). Reducing injection numbers and duration of up-dosing phase is one lever for improving the adherence of AIT. The present trial investigated the safety and tolerability of an accelerated up-dosing scheme of subcutaneous AIT(SCIT) with a native house dust mite (HDM) allergen extract in children with moderate to severe allergic rhinitis or rhinoconjunctivitis with or without asthma in China.

Method: This was a multicenter, open label, randomized and controlled trial. Children aged 5-14 years with moderate to severe allergic rhinitis or rhinoconjunctivitis with or without asthma from 3 hospitals were included. All children were 1:1 randomized to one strength group and standard group. The dose escalation scheme for patients in the one strength group included 6 injections with strength 3, whereas the standard group comprised 14 injections with strength 1, 2, and 3. Both treatment groups received 2 additional injections of the maintenance dose. All treatment-emergent adverse events (TEAEs) were recorded and analyzed. The 5-point Likert scale was used to assess the tolerability.

Results: 101 patients aged 7.3±2.37 years were included in the final analysis (One strength: 50 vs. Standard: 51). In 10% of the patients in the one strength group and in 11.8% of the standard group TEAEs occurred. There were no serious TEAEs in both treatment groups. Local reactions were reported in 1 patient in the one strength group and in 4 patients in the standard group. Systemic allergic reactions (SR) were comparable in both groups (one strength: 5 vs. standard: 4). 94.0% (47/50) of patients in the one strength group reached the maintenance dose without dose adjustment due to adverse events, compared to 96.1% (49/51) in the standard group. 100% of patients who completed the dose escalation phase reached 1.0 ml of strength 3. Tolerability was assessed by investigators and patients as "good" or "very good" in 45 (90.0%) and 44 (88.0%) patients in the one strength group and in 43 (84.3%) and 42 (82.3%) patients in the standard group, respectively.

Conclusion: The accelerated dose escalation scheme using only one strength with 6 injections of an unmodified HDM preparation is as safe and tolerable as the standard dose escalation scheme in Chinese children with moderate to severe allergic rhinitis or rhinoconjunctivitis with or without asthma. The accelerated dose escalation scheme offers the opportunity for a faster up-dosing period suitable to increase adherence to AIT therapy.

Conflicts of interest: The authors did not specify any links of interest.

100043 | Presentation of the ACESO-trial design, a randomized, placebo-controlled, double-blind trial evaluating the efficacy, tolerability, and safety of a novel delivery-system (ESO-101) for topical esophageal treatment

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*Presenting author: A. J. Lucendo Villarín

Background: Eosinophilic esophagitis (EoE) is an increasingly prevalent esophageal disease and the leading cause of dysphagia and food impaction in children and young adults. EoE results in a substantial reduction of quality of life and long-standing untreated disease leads to esophageal remodeling and strictures. The chronic natural course of EoE indicates that effective and safe treatments are mandatory, and there remains a need for esophageal-specific medication. Topical-administrated drugs have demonstrated superiority compared with systemically acting ones, but methods to deposit active compound must be developed and tested.

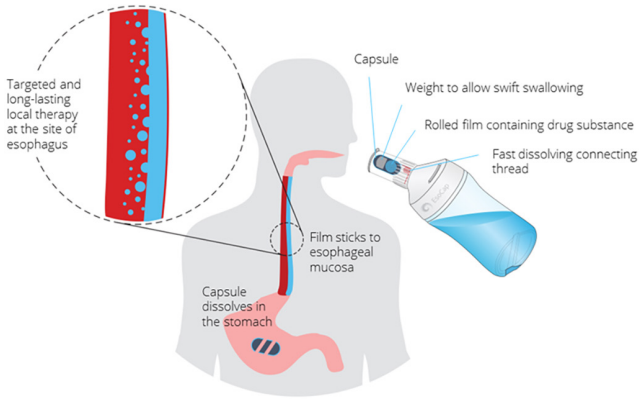
Method: ESO-101, a novel, innovative drug delivery system, targets the esophageal mucosa by significantly increasing topical contact time through a slow release of the drug mometasone furoate. This innovative application technology consists of a drug-loaded thin-film rolled up in a capsule that unravels and sticks to the esophageal mucosa when swallowed (Figure 1). This ensures local drug delivery and prolonged mucosal contact as the film slowly dissolves and delivers mometasone. The drug and delivery system are being tested in the ACESO study, a multicenter, randomized, placebo-controlled, double-blind phase II trial. Outcomes will include histological efficacy (focusing on the eosinophilic infiltration), tolerability, and safety of ESO-101 in adult patients with active EoE. Patients will be screened for active clinicopathological EoE at 2 visits (Visit 1 and Visit 2) during which their eligibility will be assessed based on the clinical symptoms and histologic assessment of esophageal biopsy samples. Eligible patients will be randomized 2:1 to once-daily treatment with ESO-101 or placebo and treated for 28 days. During the end of the treatment visit on Day 28, the primary efficacy endpoint will be evaluated by assessing the absolute change in peak eosinophil count from baseline. In addition, a safety follow-up call will be scheduled 2 weeks after the end of treatment.

Results: No results available yet.

EudraCT 2020-000082-16.

ClinicalTrials.gov Identifier: NCT04849390

Conclusion: We consider our study protocol to be suitable to demonstrate the benefit of a novel drug delivery system, designed to increase mucosal contact time and esophageal drug deposition in patients with symptomatic and active histologic EoE in a clinical phase II trial.



The EsoCap drug delivery system: The drug delivery platform comprises a slit capsule, a rolled-up thin film, a sinker, and a connecting thread. The patient swallows the capsule with a specially designed drinking device filled with water.

Conflicts of interest: Isabelle Racamier is CEO of EsoCap Biotech who sponsored the clinical ACESO study

100147 | Profile of peanut allergens sensitization and its cross-reactivity in Brazil

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*Presenting author: B. C. Ramos

Background: Peanut allergy is responsible for significant morbidity in children. Its diagnosis is based on the clinical history of a reaction to peanut ingestion, aided by the serum allergen-specific IgE (sIgE). Nonetheless, sensitization can be present as a cross-reactivity to other allergens. Our objective was to describe the peanut sensitization profile and investigate possible PR10 and LTP cross-sensitization in Brazil.

Method: Data was collected from a previous study (PROAL) that included 470 individuals. For the present study, only participants with whole-peanut and/or components (Ara h 1, Ara h 2, Ara h 3, Ara h 8, and Ara h 9) sIgE ≥0.35 kU_A/L (FEIA) were included. Also, the ImmunoCAP ISAC of 271 participants was analyzed for sensitization to peanut allergens, PR10 and LTP. Clinical characteristics like sex, age, principal allergy condition, concomitant allergy disease, and total serum IgE were assessed.

Results: From the 470 PROAL participants, 97(20.6%) had whole-peanut and/or components ≥0.35 kU_A/L. Amongst 87 peanut positive, 40(45.9%) had positivity only for peanut sIgE, 22(25.2%) for Ara h 1, 29(33.3%) for Ara h 2, 28(32.1%) for Ara h 3, 17 (19.5%) for Ara h 8, 24(27.5%) for Ara h 9. Atopic Dermatitis (AD) was present in 44.3% as the principal allergy condition, followed by food allergy (28.8%), asthma/rhinitis (15.4%), and wheezing (3%). 8 participants were healthy controls. Three participants had a history of peanut allergy, and two of them also had AD as the main condition. 48 had

their sample analyzed by ISAC and 39 had no positivity in any Ara, LTP, or PR10, 7 were Ara positive, and two were Ara negative but positive for LTP/PR10. Interestingly, 29 individuals from the PROAL had positivity in ISAC but were negative in ImmunoCAP. The LTP allergen most frequent was Pru p 3, followed by Ara h 9, Pla a 3, Par j 2. Only 4 participants had positivity in PR10 allergens, Cor a 1.0401 positive in three of them.

Conclusion: In Brazil, sensitization to peanut storage proteins are common. Cross-sensitization was mostly due to LTP then PR-10.

Conflicts of interest: The authors did not specify any links of interest.

100238 | Timing of introduction of complementary foods for early childhood allergy prevention: An overview of systematic reviews

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*Presenting author: C. Apfelbacher

Background: An increasing number of systematic reviews (SRs) is synthesising evidence to examine the effects of timing of complementary foods (CF) on the occurrence of allergic sensitization and disease. To aid medical decision making, overviews of SRs have been suggested for situations where a significant number of SRs with similar objectives are available. We therefore conducted an overview of SRs to summarise and critically appraise the existing systematic review evidence on the effects of timing of CF to prevent allergy/allergic disease. The overview will be updated regularly to provide living systematic evidence.

Method: A systematic search of four databases (e.g. PubMed (MEDLINE), Embase, Cochrane Library) was conducted up to February 2023. Outcomes included the risk of developing food allergy, allergic sensitisation, asthma, allergic rhinitis, atopic eczema, and adverse events, based on RCT evidence. At least two independent reviewers performed the screening, data extraction, risk of bias and quality assessment. The methodological quality of the included reviews was assessed based on the AMSTAR-2 tool and risk of bias (ROB) was evaluated using the ROBIS tool. ROB of primary studies within reviews was re-assessed by using the ROB 2.0 tool of the Cochrane Collaboration for primary outcomes. Results were summarised narratively and the certainty of evidence was provided based on the GRADE approach.

Results: A total of eleven SRs containing RCT evidence were included. Most of the reviews were at critically low or low methodological quality and at high risk of bias. The early introduction of peanut or cooked egg probably reduces the risk of peanut allergy (very low to low certainty evidence) or egg allergy (very low to moderate certainty evidence), respectively. Results for other atopic diseases were often inconclusive and characterized by several methodological limitations. The occurrence of adverse events was rarely examined in a systematic manner.

Conclusion: The eligibility criteria of the systematic reviews varied with respect to the timing of introducing CF, the nature of CF and the population risk, which complicated deriving conclusions across reviews. For developing guidelines to support decision-making on the timing of introducing CF as preventive strategy, the early introduction of egg and peanut seems promising whereas more extensive research is required regarding other allergic outcomes and potential harms.

Conflicts of interest: The authors did not specify any links of interest.

100461 | Is there a food induced immediate response of the esophagus "FIRE" in teens with eosinophilic esophagitis?

G. Koken[1]; HI. Ertoy Karagol[1]; S. Polat Terece[1]; Z. Cavdar[1]; K. Cetin[1]; O. Egritas Gurkan[2]; S. Sari[2]; B. Dalgic[2]; A. Bakirtas[1]

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*Presenting author: A. Bakirtas

Background: A new phenomenon has been described in adult eosinophilic esophagitis (EoE) patients called food-induced immediate response of the esophagus (FIRE). It is suspected in the presence of unpleasant symptoms that occur suddenly on contact of the triggering food with the esophageal surface and recur with repeated exposures to the same food. FIRE can often be mistaken for and coexist with pollen-food allergy syndrome (PFAS), so it is important to differentiate between the two. In this study we aimed to explore the incidence and clinical manifestations of FIRE in teens aged ≥12, as well as to identify the specific food triggers.

Method: Patient records were used to collect demographic data. Patients and their families were interviewed in person or by phone using a questionnaire to inquire about the symptoms and characteristics of FIRE and PFAS. Skin prick tests were done on suspected patients to identify the triggering foods. FIRE is defined as suitable clinical symptoms with suspected food allergen sensitization.

Results: Fifty patients (male 82%) were included in the study. Eleven of these patients with a median age: 18.2 years old (12.7–21.7) described unpleasant and recurrent symptoms that were distinct from dysphagia with certain foods. All of them had concomitant allergic rhinitis. The most frequently reported symptoms were oropharyngeal itching and tingling, with the most common triggering foods being kiwi, hazelnut, banana, and eggplant, in that order. The median time from food ingestion to symptom onset was 7 min (range: 1–30 min), and the median duration of symptom relief was 25 min (range: 10–30 min). PFAS was considered in 10/50 patients (20%) and FIRE in only one patient (%2).

Conclusion: So far, FIRE has been reported in eight adult cases and one pediatric case. In our series of teens with EoE, nearly all cases

of recurrent unpleasant symptoms related to food were associated with PFAS, with only one case exhibiting clinically compatible findings with FIRE.

Conflicts of interest: The authors did not specify any links of interest.

100512 | The long-term impact of the COVID-19 pandemic on children with eosinophilic esophagitis

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*Presenting author: A. Bakirtas

Background: There is no comprehensive study evaluating the impact of the COVID-19 pandemic specifically on children with eosinophilic esophagitis (EoE). This study therefore aimed to assess the effects of the COVID-19 pandemic on children with EoE during the first two years, including the impact on disease follow-up, treatment compliance, COVID-19 infection, and vaccination status.

Method: Treatment compliance, symptoms, endoscopic and pathological findings were compared between the last visits before the pandemic and those within the first and second years of the pandemic. Additionally, the COVID-19 infection and vaccination status were evaluated in children diagnosed with EoE. COVID-19 infection was determined by a positive PCR test.

Results: The study included 66 children with a median age of 13.2 years (min–max: 4.4–17.8 years) with EoE. The percentage of children receiving any treatment for EoE before, in the first and second year of the pandemic were 51.5%, 34.8% and 27.3%, respectively ($p < 0.01$). In the first two years of the pandemic, two patients experienced food impaction, one of whom required emergency endoscopy, while the other was relieved by vomiting. None of the patients developed a stricture. The percentage of patients who underwent at least one endoscopy before, in the first and second year of the pandemic were 72.7%, 13.6% and 33.3%, respectively ($p < 0.001$). Twenty-two patients underwent endoscopy both before and during the first or second year of the pandemic (33.3%). The increase in total EREFS scores was significant (p: 0.039) while the increase in tissue peak eosinophilia was not significant ($p > 0.05$). There was no difference in EoE symptoms ($p > 0.05$). In the first two years of the pandemic, 66.7% of children received at least one dose of COVID-19 vaccine. Twenty-four children had COVID-19 infection (36.3%), either with asymptomatic or mild clinical symptoms in 95.8% of them.

Conclusion: Despite significant disruptions to treatment compliance and endoscopic follow-ups and insignificant increase in tissue eosinophilia counts, no strictures developed in children with EoE due to COVID-19 pandemic. Almost all EoE children with COVID-19 were either asymptomatic or had mild symptoms without severe illness.

Conflicts of interest: The authors did not specify any links of interest.

100531 | Assessment of allergy immunotherapy efficiency by quantification of conjunctival provocation tests with artificial intelligencebased tools "AllergoEye"

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*Presenting author: Y. Yarin

Background: The previously reported AI based platform for quantitative analysis of conjunctival provocation tests (CPT), "AllergoEye", was applied for assessment efficiency of 12 months of immunotherapy for 25patients against rhinoconjunctivitis

Method: The immunotherapy of 25patients with grass, birch and mite rhinoconjunctivitisallergy (CAP class from 0 to 5) was performed in a monocentral prospective design. The patients were subcutaneously and sublinguallytreated according to protocols recommended by manufacturers. For each patient the CPTs were performed before therapy and at 3, 6 and 12 months during the therapy. The CPT was performed by sequential application of 4 dilutions of the allergen solution. The allergic reaction was measured by AllergoEye as well as by standardized CPT protocol, i.e. subjective (itching, irritation and tearing) and objective (RMS-redness evaluated by medical staff) reactions were documented. The hyposensitizationof patients wasevaluated by comparison of dilutionswhich triggeredanallergic reaction before and after 1 year of therapy.

Results: We found thatthenumber of patients with strong hyposensitizationwas the same as measured by AllergoEye and SSS. However, AllergoEye detected more subtle hyposensitizationthan subjective scores

Conclusion: AllergoEye is more sensitive than standard CPT scores (SSS) in line with the previously published validation study. Therefore, AllergoEye allows detect subtle hyposensitizationeffects, which could be missed otherwise. Following the therapy it is required to find, whetherreported difference in subtle hyposensitizationis predictive for responder/non-responder discrimination, which could be suggestive for therapy strategy. AllergoEye is a sensitive tool for therapy control of hyposensitizationin clinical practice and, especially, for evaluation of medication efficiency in clinical studies.

Conflicts of interest: The authors did not specify any links of interest.