Eastern Allergy Conference
June 1-4, 2023 ~ Palm Beach, FL

Scientific Posters F1-F32 will be on display in the Ponce Foyer during the coffee break, 10:00-11:00am, Friday June 2, 2023

Not for CME Credit

F1

Addressing Acute Bronchitis Readmissions at the James A. Haley Veterans Administration Hospital Emergency Department

Leah L. Ishmael, Andrew J. Cooke, Dennis K. Ledford

Introduction: Acute bronchitis is a self-limited condition, however presentation to the emergency department (ED) is often managed with oral corticosteroids, antibiotics, and short-acting beta agonist (SABA) to manage comorbid asthma and/or chronic obstructive pulmonary disease (COPD). According to the Centers for Medicare & Medicaid Services (CMS), the national ED 30-day readmission rate for acute bronchitis is 12.8%. The purpose of this study is to determine whether the addition of an inhaled corticosteroid/long-acting beta agonist (ICS/LABA) used as needed would reduce 30-day readmissions for acute bronchitis at the James A. Haley Veterans Administration Hospital (JAHVA) ED.

Methods: 30-day readmission rate for acute bronchitis at the JAHVA ED was determined through retrospective chart review from 2018 to 2019. A protocol was then implemented for identification and treatment of acute bronchitis. Veterans were recruited from October 2022 to April 2023. 18 participating veterans received either standard of care (control group) or standard of care plus ICS/LABA (treatment group). Participating veterans are actively being followed for acute bronchitis readmissions.

Results: 30-day readmission rate for acute bronchitis at the JAHVA was 12.83%. 4 of 11 participants in the control group had 30-day readmissions for acute bronchitis. None of the 7 participants in the treatment group had 30-day readmissions for acute bronchitis. 2 of the 4 participants in the control group that were readmitted received an ICS/LABA upon readmission and remained out of the ED to date.

Conclusions: Addition of an ICS/LABA as needed reduced 30-day readmissions for acute bronchitis in a small subset of patients at the JAHVA ED. Recruitment of additional participants is ongoing to further validate these findings. We suspect that a portion of patients presenting with acute bronchitis symptoms have undiagnosed asthma and/or COPD. Implementation of an ICS/LABA, followed by close clinical follow up may lead to recognition of airway disease and reduction in ED readmissions.

F2

Understanding of Severe Combined Immunodeficiency and Carrier Status in the U.S.-Based Irish Traveler Population

Silpa T. Taunk, David E. Potts, Jennifer Heimall, Stanton Goldman, Jolan E. Walter

Introduction: The Irish Travelers are an ethnically distinct minority community originating from Ireland with substantial immigration to the U.S. Given the history of cultural endogamy in this community, there are known increased rates of severe combined immunodeficiency (SCID), with two recombinase activating gene 1 pathogenic variants (*RAG1*; p.Arg897*and p.Ser259Alafs*5) and one novel non-homologous end-joining 1 gene variant (*NHEJ1*; p.Gln224Argfs*27) detected in the US community. However, knowledge of rare genetic disorders, including how they are passed and the value of carrier testing, is limited among some members of this population.

Methods: A multi-institutional collaboration developed an outreach project for SCID patients and their relatives in the U.S.-based Irish Traveler community. SCID patients were identified through newborn screening and pedigree interviews. Genetic testing for SCID variants was offered to kindred members, prioritizing members of child-bearing age. An online educational program was designed to identify knowledge gaps and disseminate information on SCID and implications of carrier status.

Results and Discussion: Baseline knowledge and attitude assessments prior to educational intervention were obtained from 28 kindred members, all of whom were female and the majority (n=23) were of child bearing age. Similar to their counterparts in Ireland, the majority (n=21) had less than a high school diploma. 12 respondents identified three or more family members diagnosed with SCID. The majority of respondents (n≥17) strongly agreed on the importance of knowing what diseases run in their family. Open ended discussions with key members of this kindred also helped identify religious and cultural barriers which contributed to hesitancy around genetic testing in this underserved community. Early diagnosis of affected members, enabled by educational sessions and carrier screening within this high-risk population, is vital to increase preparedness for the birth of a child with SCID.

F3

Prehospital Epinephrine Administration is Associated with Decreased Odds of a Biphasic Reaction and Decreased ED Length of Stay but not Decreased Hospitalization in Emergency Department Patients with Anaphylaxis

Andrea L. Hlady, MD, PhD, Aliza Weinman, MD, Yuedan Zhang, MD, Aidan F. Mullan, MA, Ronna L. Campbell, MD, PhD

Introduction: Prompt epinephrine administration is important to improve outcomes in patients with anaphylaxis. We evaluated patient characteristics and outcomes associated with prehospital epinephrine administration in emergency department (ED) patients with anaphylaxis.

Methods: We included the first visit among patients who provided consent and met anaphylaxis diagnostic criteria and excluded patients who had onset of symptoms in a healthcare facility or received no epinephrine. ED disposition was categorized as admission (hospital or intensive care unit) or dismissal. Associations were assessed with univariable logistic regression. Multivariable logistic regression (adjusting for patient age, sex, history of anaphylaxis or asthma, total comorbidities, prior epi pen prescription, EMS arrival, exposure to a known allergen, and type of allergy trigger) was also performed for the association with ED disposition.

Results: A total of 1107 patient visits were included for analysis. The median patient age was 29 (IQR 14-50), 53.6% of patients were female, 33.1% were under 18 years of age. Patients who received prehospital epinephrine were more likely to have a history of prior anaphylaxis (OR 2.78, 95% CI 2.12-3.64), a history of asthma (OR 1.48, 95% CI 1.12-1.96), and a history of food allergy (OR 1.95, 95% CI 1.52-2.51). Patients who received prehospital epinephrine were less likely to experience a biphasic reaction (OR 0.56, 95% CI: 0.34–0.92) and had a decreased ED length of stay (4.0 hours versus 4.7 hours, p<.001). There was no difference in hospital admission between patients with and without pre-hospital epinephrine in both the univariable (OR 1.30, 95% CI: 0.94–1.79) and multivariable (OR 1.30, 95% CI: 0.85–1.99) models.

Conclusions: This study demonstrates that while prehospital epinephrine administration did not reduce hospitalization in ED anaphylaxis patients, it did reduce the odds of a biphasic reaction and decreased ED length of stay.

F4

Single center experience with egg oral food challenges in the outpatient setting

Nicole Koutlas, MD, Amy Stallings, MD, Julie Kim-Chang, MD, Cynthia Zhou, MD, Talal Mousallem, MD

Introduction: Oral food challenges (OFC) remain the gold standard for diagnosing food allergy (FA). Egg is a common childhood FA, with most tolerating baked egg. We sought to characterize outcomes of plain and baked egg OFCs.

Methods: We completed a retrospective chart review of all OFCs for IgE-mediated FA in Duke University Pediatric Allergy clinics from June 2017 through May 2022. Typically, patients were deemed eligible for OFC if sIgE ≤2kU/L and skin prick test (SPT) ≤5mm, with the exception of baked egg/milk challenges.

Results: Of 663 OFCs in 510 patients (59% male), the most common foods challenged were peanut (26%), plain egg (23%), baked egg (8%) and milk (8%), with pass rates of 84%, 88%, 62% and 84%, respectively. Twenty-six (4%) OFCs were inconclusive due to inability to eat the full serving, with half occurring in egg challenges and 76% in children ≤3 years. Baked egg had the lowest pass rate, with higher failure rates among those <2 years (24% vs 12%). While urticaria was the most common reaction for all allergens (60-92% failed OFC), gastrointestinal reactions were also common among baked egg challenges, in contrast to other allergens (47% vs 0-8%). Additionally, baked egg challenges had the highest rate of multi-systemic reactions (9% vs 0-3%) and treatment with epinephrine (5% vs 0-2%) when compared to other top allergens. Within our restricted cohort, SPT and sIgE level was not associated with OFC outcome. Ovomucoid sIgE was undetectable in half of failed baked egg challenges, including in two with multi-systemic reactions.

Conclusions: Baked egg challenges had the lowest pass rate, in part due to selection bias, but also illustrating difficulties of OFCs in young children. Additionally, the lower pass rate may be attributed to suboptimal negative predictive value of ovomucoid and the potential for allergenic epitope(s) not currently routinely measured.

F5

Real-world effectiveness of dupilumab in atopic dermatitis: Consistency in rate and magnitude of improvement across observational study methodologies

Jerry Bagel, MD, Tien Q. Nguyen, MD, Eric Simpson, MD, Hermenio Lima, PhD, Dimittri Delevry, PharmD, Chien-Chia Chuang, PhD, Debra Sierka, PharmD, Moataz Daoud, PharmD, Andrew Korotzer, PhD

Introduction/Background: Results from real-world (RW) observational studies may be influenced by differences in study recruitment, design, and clinical practice. Consistent results across RW studies support generalizability of findings.

Objective: To summarize patient-reported outcomes in the RELIEVE-AD (doi:10.1001/jamadermatol.2021.4778) and PROSE (NCT03428646) RW studies of dupilumab in atopic dermatitis (AD).

Method: RELIEVE-AD was a prospective, observational, RW study of dupilumab effectiveness in patients (pts) with moderate-to-severe AD recruited from a US patient support program. PROSE is a prospective, observational, multicenter registry of AD pts initiating dupilumab in the US and Canada. Skin pain, heat/burning, and skin sensitivity numeric rating scale (NRS; each scale 0–10) and Dermatology Life Quality Index (DLQI; 0–30) were compared between studies.

Results: In RELIEVE-AD (N=698)/PROSE (N=764), mean age was 46/41 years, 62%/59% female, 74%/55% white. Trajectory of improvement with dupilumab was similar between RELIEVE-AD/PROSE: mean skin pain NRS improved from 5.9/5.4 at baseline (BL) to 2.3/2.3 at Month (M) 2, and 1.7/1.7 at M12; heat/burning NRS improved from 5.2/4.7 at BL to 1.9/2.0 at M2, and 1.5/1.6 at M12; skin sensitivity NRS improved from 5.5/5.2 at BL to 2.0/2.3 at M2, and 1.5/1.8 at M12; and DLQI improved from 14.4/13.3 at BL to 4.8/5.9 at M3, and 3.5/5.1 at M12.

Conclusions: Two RW studies utilizing different methodologies yielded similar findings regarding time course and extent of dupilumab effectiveness in AD across multiple patient-reported outcomes.

Funded by Sanofi and Regeneron Pharmaceuticals Inc.

F6

Long-Term Safety in Adults with Moderate-to-Severe Atopic Dermatitis Treated with Dupilumab up to 4 years

Andrew Blauvelt, MD , Lawrence F. Eichenfield, MD , Debra Sierka, PharmD, Zhen Chen, PhD, Faisal A. Khokhar, MD, Ainara Rodríguez Marco, MD, Arsalan Shabbir, PhD

Introduction: In patients with atopic dermatitis (AD), classical immunosuppressive treatments are not recommended for continuous use due to safety concerns. This analysis reports long-term safety of dupilumab up to 4 years in adults with moderate-to-severe AD.

Methods: In the LIBERTY AD OLE (NCT01949311) study, adult patients ≥18 years old with AD initially received dupilumab 300mg weekly. 226 ongoing patients transitioned to 300mg every other week (q2w) to align with approved dosing. Use of topical corticosteroids (TCS) or calcineurin inhibitors was permitted. Treatment-emergent adverse events (TEAE) are reported as number of patients per 100-patient years (nP/100PY). Due to the lack of a control arm, LIBERTY AD CHRONOS (NCT02260986) 52-week safety results are provided.

Results: 2,207/1,065/557/362/352 patients completed up to 52/100/148/172/204 weeks of treatment. Mean (SD) treatment exposure was 103.4±57.8 weeks. Of the 2,677 patients included in the analysis, 2,273 experienced ≥1 TEAE (167.5 nP/100PY), which were mainly mild or moderate, and were lower than in the 300mg weekly + TCS arm of the 1-year CHRONOS trial (322.4 nP/100PY). 99 patients (1.8 nP/100PY) experienced TEAEs leading to treatment discontinuation. Of 536 patients reporting ≥1 event of conjunctivitis, 95% had mild (4.7 nP/100PY) or moderate (5.0 nP/100PY) severity. 89% of conjunctivitis events were resolved or resolving, and 0.5% (0.2 nP/100PY) led to treatment discontinuation. Efficacy was sustained and consistent with previous reports of this study.

Conclusion: The overall safety profile of dupilumab up to 4 years was consistent with the known safety profile and demonstrated sustained efficacy in adult patients with moderate-to-severe AD.
.

Funded by Sanofi and Regeneron Pharmaceuticals Inc.

F7

Dupilumab Improves Histologic and Endoscopic Aspects of Eosinophilic Esophagitis in Children Aged 1 to 11 Years in the Phase 3 EoE KIDS Trial

Mirna Chehade, MD, Evan S. Dellon, MD, Jonathan M. Spergel, MD, Marc E. Rothenberg, MD, Ruiqi Liu, PhD, Leda P. Mannent, MD, Elizabeth Laws, Phd, Eric Mortensen, MD, Jennifer Maloney, MD, Faisal A. Khokhar, MD, Lila Glotfelty, MD, Arsalan Shabbir, MD

Introduction: There are no approved eosinophilic esophagitis (EoE) treatments in children <12 years. Dupilumab, a human mAb, blocks interleukin-4/interleukin-13, central drivers of type-2 inflammation in EoE. In the phase 3 LIBERTY-EoE-TREET study, dupilumab improved histologic, symptomatic, and endoscopic outcomes and was well tolerated in adolescents and adults.

Aim: Part A of the phase 3 EoE KIDS trial (NCT04394351) evaluated dupilumab efficacy, safety, and tolerability vs placebo in patients aged 1–11 years with active EoE for 16 weeks.

Methods: Participants (n=102) were randomized to receive subcutaneous dupilumab at a weight-tiered, higher-dose (n=37), lower-dose (n=31), or matching placebo (n=34). Inclusion criteria: diagnosis of EoE unresponsive to proton pump inhibitor and baseline esophageal eosinophil (eos) count ≥15eos/high-power field (hpf) in ≥2 regions. Exclusion criteria: bodyweight <5kg or ≥60kg; eosinophilic gastroenteritis; non-EoE causes of esophageal eosinophilia.

Results: At week 16, 68% and 58% on higher- and lower-dose dupilumab achieved primary endpoint of peak esophageal eos count (PEC) ≤6eos/hpf, vs 3% on placebo (both $P<0.0001$). Children on higher-dose dupilumab experienced the following changes: –86% in PEC vs +21% for placebo ($P<0.0001$); –0.88 and –0.84 in Histologic Scoring System grade and stage scores, respectively, vs +0.02 and +0.05 for placebo (both $P<0.0001$); –3.5 in Endoscopic Reference Score vs +0.3 for placebo ($P<0.0001$); improvement in % days experiencing ≥1EoE signs; +3.09-percentile in bodyweight vs +0.29 for placebo. Changes in histologic and anatomic outcomes were comparable in the lower-dose group (all nominally significant vs placebo). Rates of AEs were 79% for dupilumab and 91% for placebo. AEs more commonly observed with dupilumab included COVID-19, rash, and headache.

Conclusion: This phase 3 trial met its primary endpoint of histologic disease remission at 16 weeks with both doses. Dupilumab higher-dose also demonstrated significant and clinically meaningful changes in additional histologic and endoscopic outcomes and improvements in symptoms and weight

Funded by Sanofi and Regeneron Pharmaceuticals Inc.

F8

Dupilumab Improves Clinical, Symptomatic, Histologic, and Endoscopic Aspects of EoE up to 24 Weeks: Pooled Results From Parts A and B of Phase 3 LIBERTY-EoE-TREET

Evan S. Dellon, MD, Marc E. Rothenberg, MD, Albert J. Bredenoord, MD, Alfredo J. Lucendo, MD, Ikuo Hirano, MD, Xian Sun, PhD, Kiran Patel, MD

Introduction: Eosinophilic esophagitis (EoE) is a chronic, progressive, type 2 inflammatory disease of the esophagus. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin(IL)-4/IL-13, central drivers of type 2 inflammation. Here we report the pooled results from Parts A and B of the three-part, randomized, placebo-controlled phase 3 LIBERTY-EoE-TREET study (NCT03633617) which evaluated the efficacy and safety of weekly dupilumab 300 mg vs placebo in adults and adolescents with EoE.

Methods: Patients were randomized 1:1 to dupilumab (n=122) or placebo (n=118). Endpoints (all at Week 24) were: proportion of patients achieving peak eosinophil count ≤6/high-power field (hpf); absolute and percent change in Dysphagia Symptom Questionnaire (DSQ) score; % change in peak eosinophil count; absolute change in Histologic Scoring System (HSS) grade and stage scores and Endoscopic Reference Score (EREFS); proportion of patients achieving peak eosinophil count <15/hpf. Nominal *P*-values are reported for this post-hoc analysis.

Results: Baseline characteristics were comparable between treatment groups. More patients treated with dupilumab versus placebo achieved peak eosinophil count ≤6/hpf (59.0% vs 5.9%; $P<0.0001$). Dupilumab treatment resulted in greater absolute (least squares [LS] mean –23.2 vs –12.7; LS mean difference [95% confidence interval] –10.5 [–14.5, –6.6]; $P<0.0001$) and percent (–65.5% vs –38.3%; –27.3 [–38.2, –16.2]; $P<0.0001$) change in DSQ vs placebo. Dupilumab vs placebo had a greater percent change in peak eosinophil count (–80.1 vs 1.5; –81.7 [–96.2, –67.1]); proportion of patients achieving <15 eos/hpf (77.0% vs 7.6%); change in HSS grade (–0.82 vs –0.1; –0.71 [–0.81, –0.62]) and stage (–0.79 vs –0.09; –0.70 [–0.79, –0.61]) scores; and change in EREFS score (–3.95 vs –0.41; –3.54 [–4.27, –2.81]); all $P<0.0001$. Dupilumab was generally well tolerated.

Conclusions: Dupilumab improved clinical, symptomatic, histologic, and endoscopic aspects of EoE and was well tolerated.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F9

Dupilumab Treatment of Children with Moderate-to-Severe Atopic Dermatitis Increases Bone Alkaline Phosphatase, a Marker of Bone Mineralization

Alan D. Irvine, MD, Amy S. Paller, MD, Sara Hamon, PhD, Julie Horowitz, PhD, Annamaria Farrell, Sarah Hatsell, PhD, Ainara Rodríguez Marco, MD, Ashish Bansal, MD, Zhen Chen, PhD, Sonya L. Cyr, PhD

Introduction: Compared to healthy children, children with moderate-to-severe AD have a risk of lower bone alkaline phosphatase (BALP) and bone mineral density (BMD). This could contribute to a higher lifetime prevalence osteopenia and osteoporosis in patients (pts) with AD.
Objective: To report the impact of dupilumab (DPL) treatment on BALP, a markers of bone formation, in children with moderate-to-severe AD.

Methods: The analysis was performed retrospectively on sera from participants in LIBERTY AD PEDS (NCT03345914) and LIBERTY AD PED-OLE (NCT02612454). In LIBERTY AD PEDS, a double-blind, 16-week, phase 3 trial, children (6–<12 years) were randomized 1:1:1 to 300mg dupilumab every 4 weeks (q4w), weight-based dupilumab every 2 weeks (q2w; baseline [BL] weight <30kg: 100mg; ≥30kg: 200mg), or placebo (PBO); with topical corticosteroids (TCS). Children (6–<12 years) were then enrolled in the open-label extension study. Pts received dupilumab 300mg q4w, with possible up-titration in case of inadequate clinical response at Week 16 (<60kg: 200mg q2w; ≥60kg: 300mg q2w); with TCS. The bone biomarker BALP was analyzed at BL, 8, 12, 16 and 52 weeks.

Results: Dupilumab rapidly and significantly increased geometric mean (standard error) levels of BALP at 16 weeks vs PBO (77.7(1.02)µg/L vs 65.0(1.04)µg/L; P<0.0001), and BALP levels in children from the PBO group once they joined the OLE. BALP levels increased over 52 weeks in all children, reaching 78–84µg/L, constituting significant improvement vs BL and reference intervals.

Conclusions: These results show a rapid and significant increase in BALP in children with AD during treatment with dupilumab, suggesting increased bone mineralization.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F10

Dupilumab is effective in children (6–11 years) with moderate-to-severe asthma and high eosinophils at baseline

Daniel J. Jackson, MD, Eckard Hamelmann, MD, Graham Roberts, DM, Leonard B. Bacharier, MD, Arman Altincatal, Rebecca Gall, MD, Olivier Ledanois, MD, Juby A. Jacob-Nara, MD, Amr Radwan, MB, Paul J. Rowe, MD, Yamo Deniz, MD

Background: Children with moderate-to-severe asthma often remain symptomatic despite standard-of-care treatments. Also, the patients with elevated peripheral eosinophil levels frequently have increased rates of exacerbations and worse asthma control. In the phase 3 LIBERTY ASTHMA VOYAGE study (NCT02948959), treatment with dupilumab, a fully human monoclonal antibody that blocks the shared receptor component for IL-4 and IL-13, was generally well tolerated and resulted in fewer exacerbations and improved lung function vs placebo in children aged 6–11 years with uncontrolled moderate-to-severe asthma. This post hoc analysis investigates dupilumab efficacy in patients with baseline blood eosinophils (≥500 cells/µL) enrolled in the VOYAGE study.

Methods: Patients received add-on dupilumab (100/200 mg by body weight at randomization) or matched add-on placebo every 2 weeks (q2w) for 52 weeks. Endpoints: 1) annualized rate of severe exacerbations, and 2) least squares mean (LSM) change from baseline in pre-bronchodilator (pre-BD) percent predicted forced expiratory volume in first second ($ppFEV_1$).

Results: In patients with baseline blood eosinophils ≥500 cells/µL, add-on dupilumab significantly lowered annualized exacerbation rates (0.249 [95% CI 0.156–0.397]; n=126) compared with add-on placebo (0.749 [0.453–1.239]; P<0.001; n=48) and also significantly improved pre-BD $ppFEV_1$ vs placebo at Week 12 (LSM difference [95% CI] 6.47 percentage points [2.27–10.66]; P<0.01) and at Week 52 (LSM difference [95% CI] 7.98 percentage points [2.17–13.78]; P<0.01).

Conclusion: Dupilumab significantly reduced severe exacerbations and improved lung function vs placebo in children with moderate-to-severe asthma and baseline blood eosinophils ≥500 cells/µL.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F11

Baseline Characteristics Of Patients With Asthma Treated With Dupilumab In A Real-World Setting: The RAPID Registry

Njira L. Lugogo, MD, Xavier Soler, PhD, Andrew Menzies-Gow, MD, Anju T. Peters, MD, Andréanne Côté, MD, Ole Hilberg, MD, Changming Xia, PhD, Lucia de Prado Gomez, MSc, Paul J. Rowe, MD, Amr Radwan, MB, Juby A. Jacob-Nara, MD, Yamo Deniz, MD

Rationale: Patients with uncontrolled, moderate-to-severe asthma have higher risk for exacerbations and impaired lung function. Dupilumab is an antibody that blocks interleukin (IL)-4 and IL-13. We aimed to characterize patients with asthma initiating dupilumab, enrolled in the RAPID registry (NCT04287621).

Methods: Patients enrolled in RAPID during a 6-month period were analysed using baseline demographics, clinical and medication history, and type 2 biomarker levels.

Results: Of 205 patients enrolled; 65.4% were female, 74.1% White, 13.2% Black/African-American, and 24.4% current/former smokers. Mean (SD) age was 50.10 years (17.41); BMI was 30.67kg/m^2 (7.96); 86.8% had moderate-to-severe asthma (GINA steps 3–5). Mean (SD) severe asthma exacerbations in previous year (n=78) were 4.4 (6.44). Mean (SD) pre-bronchodilator (BD) FEV1 was 2.29L (1.14), pre-BD percent predicted FEV1 was 70.34% (20.30), forced vital capacity was 3.09L (1.08), and peak expiratory flow, 356.88L/min (169.83). Median (range) eosinophils (n=64) were 305.0 cells/□L (0–2142.0); 10 (15.6%), 15 (23.4%), 17 (26.6%), and 22 patients (34.4%) had eosinophils <150, ≥150 to <300, ≥300 to <500, and ≥500 cells/□L, respectively. Patients with any OCS use at baseline per eosinophil count were: 2 (3.1%), 3 (4.7%), 0, and 2 (3.1%) for eosinophils <150, ≥150 to <300, ≥300 to <500, and ≥500 cells/□L. Fractional exhaled nitric oxide was 42.2ppb (SD 34.83). 6-Item Asthma Control Questionnaire score was 2.40 (SD 1.18); Asthma Quality of Life Questionnaire score was 4.10 (SD 1.31).

Conclusions: This initial sample from RAPID, had predominantly female, white, overweight patients with moderate-to-severe asthma, and impaired lung function and quality of life.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F12

Bezuclastinib, a novel, selective, and potent kit inhibitor with minimal brain penetration, being evaluated in summit, a phase 2 study in patients with indolent or smoldering systemic mastocytosis

Anna Guarnieri, Cem Akin, Karyn Bouhana, Shannon Winski, Mariana Castells

Introduction Agents targeting *KIT* D816V mutation in exon 17 have been used to treat advanced systemic mastocytosis (SM), but there are no approved targeted therapies for indolent or smoldering SM (NonAdvanced SM). Limitations of available KIT therapies include off-target activity and significant brain penetration, which may cause toxicities that limit dosing and efficacy, resulting in unmet need for therapies with high selectivity and reduced brain penetration. Preliminary Phase 2 data show that type I tyrosine kinase inhibitor bezuclastinib was well-tolerated in advanced SM patients, with early signs of clinical activity. The aim herein is to explore the rationale for bezuclastinib as a therapy for patients with NonAdvanced SM.

Methods: Nonclinical studies evaluated bezuclastinib's selectivity compared to other KIT tyrosine kinase inhibitors. HMC1.2 human mast cells were used to determine IC_{50} values. Off-target assays measured phosphorylation of other proteins. *In vivo* pharmacokinetics and pharmacodynamics were assessed, and myelotoxicity potential was evaluated in a human *in vitro* colony forming assay. Brain distribution was also evaluated in rats administered bezuclastinib, avapritinib, or BLU-263 for 3 days.

Results: Bezuclastinib selectively inhibited KIT D816V *in vitro* without off-target activity. *In vivo* plasma exposure led to a 50% reduction in splenomegaly and KIT phosphorylation at doses of 3-10 mg/kg/day corresponding to exposures of 1.5-2.2 µg·hr/mL which correlated well with inhibition of pKIT in a xenograft model. *In vitro* colony forming assays showed improved myelotoxicity compared to avapritinib or ruxolitinib. The brain to plasma ratio indicated little to no CNS penetration, and rats treated with bezuclastinib showed no behavioral changes.

Conclusion: Bezulclastinib's selectivity and safety profile, including minimal brain penetration, suggest it could be a differentiated KIT inhibitor for SM. The ongoing Summit Phase 2 clinical trial (NCT05186753) aims to evaluate bezuclastinib's safety and efficacy in NonAdvanced SM patients, with the goal of addressing high unmet needs.

Funded by Cogent Biosciences

F13

Efficacy Of Biologics In Patients With Severe Allergic Asthma, Overall And By Blood Eosinophil Count

Jonathan A Bernstein, Stephanie Korn, Christopher S Ambrose, Jean-Pierre Llanos-Ackert, Gillian Hunter, Neil Martin

Introduction: Patients with uncontrolled, severe allergic asthma may be prescribed biologic therapies to reduce exacerbations and improve disease control. Randomized controlled trials (RCTs) of these therapies have differed in design, with varying results overall and by baseline blood eosinophil count (BEC). Here we describe annualized asthma exacerbation rate (AAER) reductions from RCTs in patients with severe allergic asthma overall and by baseline BEC category.

Methods: A literature search was performed to identify published phase 3 RCT data of FDA-approved biologics in patients with severe, uncontrolled asthma with confirmed allergy to perennial aeroallergens, where AAER reduction versus placebo was measured in the overall population and/or in those with a high or low BEC at baseline or screening.

Results: The serum total immunoglobulin E levels varied between biologic RCT analyses. In the overall allergic population, data were available for tezepelumab, dupilumab and omalizumab only; the greatest AAER reduction was observed with tezepelumab (58%; rate ratio: 0.42; 95% confidence interval [CI]: 0.33–0.53). In patients with allergy and BECs of at least 260 cells/μL or at least 300 cells/μL or higher, AAER reductions were observed with all biologics; the smallest AAER reduction was observed with omalizumab (32%; rate ratio: 0.68; 95% CI: 0.52–0.89). In patients with allergy and BEC less than 300 cells/μL (regardless of historical BEC), an AAER reduction was observed with tezepelumab (45%; rate ratio: 0.55; 95% CI: 0.40–0.75) but not with mepolizumab, benralizumab or omalizumab.

Conclusion: Among patients with severe allergic asthma, tezepelumab was the only biologic to demonstrate reductions consistently in AAER across all subgroups. The efficacy of biologics varies considerably overall and by BEC. These differences can inform provider treatment decisions.

Funded by AstraZeneca and Amgen Inc.

F14

Impact of Duration of Wear on Efficacy of Epicutaneous Immunotherapy with Viaskin Peanut in Toddlers 1-3 Years of Age During the Phase 3 EPITOPE Study

Todd D. Green, Katharine J. Bee, Henry T. Bahnson, Dianne E. Campbell, Hugh A. Sampson

Introduction: Viaskin™ Peanut 250 µg (VP250), a novel approach to allergen immunotherapy, is an epicutaneous system (patch) being developed for peanut allergy treatment. In the EPITOPE Phase 3 study, daily VP250 treatment resulted in statistically superior desensitization vs placebo (responder rate: 67.0% vs 33.5%) after 12 months in 1 through 3-year-old peanut-allergic toddlers. VP250 is designed to balance sufficient patch adhesion with minimizing removal pain/irritation; therefore, we aimed to characterize average daily wear time and treatment response in the study.

Methods: EPITOPE was a Phase 3, double-blind, placebo-controlled, randomized study with a protocol-specified daily wear time for VP250 of 24±4 hours. Average daily wear time was determined by assessing patch adhesion at the time of application and removal. Primary responder outcome (for subjects with non-missing outcome data) was assessed according to mean daily wear time, categorized by hours.

Results: Median average daily wear times in the EPITOPE study were 22.2 hours (VP250) and 23.7 hours (placebo). The results of the study showed a strong association between duration of wear and efficacy. Among participants with <20 hours application duration, a responder rate of 60.3% was observed, increasing to 66.7%, 84.6%, 87.0%, and 100% for those with mean durations of 20, 21, 22, and ≥23 hours, respectively. A small group of participants (10%) had low mean daily wear times, and these participants could be identified within the first 3 months of treatment.

Conclusion: EPITOPE analyses demonstrated high treatment responder rates and high mean daily wear times for the majority of VP250 participants. Mean daily wear time was strongly associated with treatment response. Low mean daily wear times were observed in a small proportion of VP250 participants, and these participants could be identified early in treatment. These results support the continued investigation of epicutaneous immunotherapy with Viaskin Peanut in peanut-allergic young children.

Funded by DBV Technologies

F15

Survey of Diagnostic Journey, Treatment Experience, and Impact on Daily Living of Patients With Alpha-1 Antitrypsin Deficiency

Alicia H. McAuliffe-Fogarty, Alina Karim, D. Kyle Hogarth, Chris Blair, Jimmy Hinson,[3]

Rationale: Limited evidence exists on the journeys of patients with alpha-1 antitrypsin deficiency (AATD), a genetic condition that can manifest as severe lung or liver disease.

Methods: PatientsLikeMe (PLM), a digital platform where patients can support and educate each other, surveyed registered US patients (aged ≥18 years) with self-reported AATD about their diagnostic journey, healthcare experience, and quality of life.

Results: Forty-three survey participants (mean[SD] age 37.0[14.6] years) said they saw 3 healthcare providers (HCPs), on average, before receiving an AATD diagnosis. Based on 24 responses, mean(SD) time from symptom onset to diagnosis was 6.9(9.3) years. Half of the participants (22/43) were diagnosed by pulmonologists. Fifty-six percent (24/23) reported finally being diagnosed due to persistent symptoms and/or ineffective medications. Most participants (35/43, 81%) felt their symptoms were well-managed. Most participants (32/43, 75%) reported having clear communication with their HCPs. Of the 35 participants setting AATD management goals, 29 received help from HCPs to set them. Seven participants reported having a positive experience with augmentation therapy. Mean(SD) score (from 35 responses) on the chronic obstructive pulmonary disease assessment test was 20.5(6.1), indicating that participants believed their symptoms hindered daily function. Shortness of breath during brisk/uphill walks was reported (Modified Medical Research Council Dyspnea Scale mean score=1). Participants generally rated their health as “good” (mean scores: EuroQol-5 Dimension-5 Level=0.6 and EuroQol Visual Analogue Scale=62.7).

Conclusions: Patients with AATD are commonly misdiagnosed for years until worsening symptoms impact their daily life. Seven out of 43 participants reported positive experiences with augmentation therapy for AATD management. Most participants reported having good communication with their HCPs and believed they could set realistic AATD management goals. Participants reported that their current symptoms, while well-managed, impacted their day-to-day lives.

Funded by Takeda Pharmaceuticals USA, Inc.

F16

The Social And Emotional Burden Of Living With Multiple Food Allergies: A Qualitative Study In The United States

Christina Ciaccio, Jessica Dunne, Andrea Bever, Alexis T Mickle, Stacey Kowal, Arpamas Seetasith, Andrew Lloyed, Karissa Johnston

Rationale: To provide insight on unmet need, this study examined the lived experiences of adults with multiple food allergies.

Methods: In this qualitative study, adults with multiple (≥2) food allergies in the United States participated in virtual semi-structured interviews (≥1 hour each) from March-April 2022. Participants were asked to describe their experiences of living with food allergies, the impact on their quality of life, and their opinions on treatment. Patterns in responses were explored using reflexive thematic analysis.

Results: Participants (n=10; mean age, 37 years) had a mean age at diagnosis of 16.5 years. Most participants were allergic to peanuts (n=7), allergic to ≥3 foods (n=7) and had experienced a severe reaction requiring an epinephrine injection (n=6) and/or a visit to the hospital/emergency room (n=6). Participants described how preparedness and allergen avoidance is time consuming, requires eating in controlled or familiar environments, and results in loss of spontaneity. Emotional impacts varied for each participant from day-to-day and varied between participants based on personal coping strategies. Participants emphasized how involvement in society requires speaking up and trusting others, which can be difficult. Participants expressed the social and cultural meaning of food, and the potential strain of allergen avoidance on relationships. Participants suggested that alternative treatment options could allow them to engage more fully in social situations.

Conclusions: Adults with multiple food allergies experience social limitations, stress about food safety, and restrictions on freedom. These findings highlight unmet need and support development of a quantitative survey.

Funded by Genentech

F17

Effect of Sex on Response to Omalizumab In Patients With Asthma

Cecile Holweg, John W. Steinke, Ben Trzaskoma, Sergio E. Chiarella, Dawn C. Newcomb, Lauren A Millette

Introduction: There are sex-related disparities in asthma. Before puberty, males have increased prevalence and severity of asthma compared with females, and this pattern reverses after the onset of puberty. Omalizumab, an IgE antibody, is an effective treatment for allergic asthma, but sex-specific responses have not been studied in detail.

Methods: Post hoc analysis examined data from randomized, placebo-controlled IA05 trial of omalizumab treatment (52 weeks; 75-375 mg sc every 2-4 weeks; N=627; 6 to <12 years, ie children) and open-label, single-arm PROSPERO study (NCT01922037; 48-weeks; N=801; ≥12 years ie adolescents/adults (n=732 ≥18 years); both included patients with moderate-severe allergic asthma.

Results:In IA05/PROSPERO, baseline characteristics of mean age and IgE levels were similar for female and male participants (females 8.4/47.8 versus males 8.6/46.2 years; IgE levels females 463.2/560.3 versus males 472.8/615.0 IU/mL). Asthma exacerbation rates following omalizumab treatment were similar for females and males. In IA05 (children), asthma exacerbation rates were: females - placebo 0.74 versus omalizumab 0.46, males - placebo 0.55 versus omalizumab 0.43, and the interaction test of effect of sex on omalizumab response was not significant (p=0.4821). In PROSPERO (adolescents/adults), asthma exacerbation rates in females were 0.74 versus males 0.77 (p=0.787). Overall safety reported previously for IA05, Lanier JACI 2009;124;1210-6 and PROSPERO, Casale JACI:IP 2019;7(1):156-64.

Conclusions: Despite differences in asthma between females and males, we found no evidence that the effect of omalizumab in children was dependent on sex, and no evidence that the rate of exacerbations was dependent on sex following omalizumab initiation in adolescents/adults.

Funded by Genentech

F18

Analysis of trough levels of total IgG, IgG subclasses, measles neutralizing antibodies and IgG antibodies to encapsulated pathogens after infusion of a 5% or 10% intravenous immunoglobulin

Kim Clark, PharmD, MBA, IgCP®, Miranda Norton, PhD, Martyn Paddick, BSc, John More, PhD

Introduction: Patients with primary immunodeficiency (PI) are at risk of infection due to low IgG levels. We report trough levels of total IgG, IgG subclasses, measles neutralizing antibody (MVab) titers, *Haemophilus influenzae* type B and seven *Streptococcus pneumoniae* serotypes in PI patients receiving a 5% and 10% intravenous immunoglobulin (IVIG) formulation.

Methods: GMX07 was a bioequivalence trial comparing Gammaplex 10% IVIG with Gammaplex 5% IVIG in patients with PI. Adult patients received the 5% for ≥ five infusions, then the 10% for ≥ five infusions, or vice versa. Pediatric patients received the 10% for 5 infusions. Doses were 300 - 800 mg/kg/infusion. Trough IgG levels were measured before each infusion. Trough levels for MVab, *H. influenzae* and *S. pneumoniae* titers were measured after the last infusion.

Results: 33 adults received the 5%, 32 received the 10%. 15 pediatric patients received the 10%. In adults, median IgG trough levels = 952.5 mg/dL for the 10% and 937.0 mg/dL for the 5%. In pediatric patients, median trough level = 879.5 mg/dL. Trough levels of IgG subclasses were comparable across formulations and age groups. Adult patients had a mean MVab titer of 2908 mIU/mL with the 5% vs 3213 mIU/mL for the 10%. In pediatric patients, mean MVab titer was 2122 mIU/mL. In adults, median trough levels of IgG antibodies to *H. influenzae* were 2.80 µg/mL for the 5% and 2.76 µg/mL for the 10%. Trough levels of IgG antibodies to all *S. pneumoniae* serotypes were consistent across formulations and age groups. No clinically meaningful differences were noted between formulations, 21-day vs 28-day regimens, or age groups.

Discussion: Maintaining IgG trough levels and mean MVab trough titers above protective thresholds is critical for patients with PI. No trough levels or titers fell below the protective thresholds. While thresholds for protective levels for *H. influenzae* or *S. pneumoniae* are not clearly defined, delivery of these antibodies to PI patients was demonstrated.

Conclusion: Our results indicate protective trough levels of IgG and antibody titers are delivered with the 5% and 10% formulations of this IVIG product, with similar results for adult and pediatric PI patients.

Funded by Bio Products Laboratory Global Medical

F19

VITESSE: phase 3, double-blind, placebo-controlled study of the efficacy and safety of epicutaneous immunotherapy in peanut allergic children aged 4-7 years

David M. Fleischer, Panida Sriaroon, Thomas Casale, Katharine J. Bee, Hugh A. Sampson

Introduction: Epicutaneous immunotherapy (EPIT) with Viaskin Peanut 250 µg (VP250) delivers microgram quantities of peanut allergen to the skin to induce desensitization.[1-4] Post-hoc analysis of PEPITES showed that VP250 was more effective in desensitizing 4-7 year-old peanut allergic children compared to those aged 8-11 years. The size and shape of VP250 have been modified (occlusion chamber and dose unchanged), and VITESSE aims to evaluate the efficacy and safety of the modified VP250 patch in peanut allergic children aged 4-7 years.

Methods: VITESSE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study. Eligible children will undergo a double-blind, placebo-controlled food challenge (DBPCFC) to peanut. Those that develop symptoms meeting stopping criteria at an eliciting dose (ED) ≤100 mg peanut protein will be randomized 2:1 to 12 months of daily treatment with VP250 or placebo. At Month (M) 12, a DBPCFC will be performed escalating to 1000 mg (2043 mg cumulative). Immunological changes, safety, and adhesion of VP250 will be assessed.

Results: VITESSE will enroll ~600 subjects. The primary endpoint is percentage of treatment responders, defined as those with a DBPCFC M12 ED ≥300 mg if baseline ED ≤30 mg, or M12 ED ≥600 mg if baseline ED >30 mg, in the VP250 group vs placebo at M12. Secondary endpoints include cumulative reactive dose and ED at M12, maximum severity of allergic reactions on DBPCFC, and percentage with a M12 ED ≥600 mg and M12 ED ≥1000 mg peanut protein. Safety assessments include adverse events, local site reactions, and systemic allergic reactions.

Conclusion: Young children have a potentially more modifiable immune system and may be more responsive to food allergen immunotherapy. VITESSE aims to evaluate the modified VP250 peanut patch in children aged 4-7 years, who are more likely to benefit from EPIT. Patient screening will begin in 2023 with topline results anticipated in 2025.

Funded by DBV Technologies

F20

EPITOPE Study Results: Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Epicutaneous Immunotherapy in Peanut-Allergic Toddlers

Matthew Greenhawt, Sayantani B. Sindher, Julie Wang, Katharine J. Bee, A. Wesley Burks

Introduction: No approved peanut allergy treatments exist for children <4 years old. This study aimed to assess the efficacy and safety of epicutaneous immunotherapy with Viaskin Peanut
250 µg (VP250) among peanut-allergic children aged 1-3 years.

Methods: In a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial (EPITOPE), peanut-allergic children developing symptoms meeting stopping criteria during double-blind, placebo-controlled food challenge (DBPCFC) at an eliciting dose (ED) ≤300 mg peanut protein were randomized 2:1 to 12 months of daily treatment with VP250 (n=244) or placebo patch (n=118). The primary outcome was the percent difference in responders between groups, determined by DBPCFC ED at baseline and Month (M)12. Maximum severity of symptoms at baseline and M12 between groups was compared. Safety was assessed by treatment-emergent adverse event (TEAE) rate.

Results: Of 362 participants randomized, 84.8% completed treatment. The primary efficacy endpoint was met by 67% receiving VP250 vs. 33.5% receiving placebo (difference=33.4%; 95% CI: 22.4–44.5% [p<0.001]). Additionally, 64.2% active vs. 29.6% placebo recipients (difference=34.7%; [p<0.001]) achieved a peanut protein ED ≥1000 mg. At baseline, an equal percentage of subjects in both groups (24.6%) had a "severe" maximum symptom severity score. At M12, there was a significant difference between groups in maximum symptom severity (p<0.001), with 12.5% active subjects compared with 28.6% placebo subjects having a "severe" symptom severity score. The majority of TEAEs were mild or moderate application site reactions. Serious TEAEs occurred in 8.6% VP250 vs. 2.5% placebo recipients, with 1.6% (n=4) VP250 subjects experiencing treatment-related anaphylaxis, and 3.3% (n=8) VP250 subjects discontinuing due to a TEAE.

Conclusions: Twelve months of epicutaneous immunotherapy with VP250 was associated with a statistically significant response vs. placebo and may reduce severity of allergic reactions among peanut-allergic children aged 1 to <4 years. Rates of treatment-related anaphylaxis and discontinuations due to TEAEs were low.

Funded by DBV Technologies

F21

Real-World Insights on the burden of Hypereosinophilic Syndrome (HES)

Anna Kovalszki, Michael E. Wechsler, Jared Silver, Brian Stone, William A. McCann, Lynn Huynh, Anamika Khanal, Mingchen Ye, Mei Sheng Duh, Arijita Deb

Rationale: HES is a group of rare hematological disorders marked by a persistently elevated eosinophil count along with tissue and organ damage. Real-world data describing characteristics and treatment patterns of HES patients managed by specialists in non-academic centers is limited.

Methods: We performed a retrospective chart review study using Electronic Medical Record (EMR) data from Allergy Partners (AP) network (2007–2021). HES patients were identified based on a clinical diagnosis of HES and an absolute eosinophil count (AEC) of >=1,500/microliter. Patients were followed longitudinally from index date (first AP visit) until end of data availability.

Results: Of the 99 HES patients identified, 52 patients met all eligibility criteria (53.8% female, 57.7% white, median age of diagnosis: 40.5 years, median age at index: 42.5 years). Half of the patients received their first HES diagnosis outside the AP network and primary care physicians were the most common referring physician (65.4%), followed by hematologist (11.5%). Rhinitis (71.2%) and asthma (44.2%) were common comorbidities. The median (interquartile range [IQR]) peak AEC was 2200.0/microliter (1700.0, 3300.5). Half of the patients reported >=15 distinct symptoms during entire study period, with >80% of the patients reporting fatigue, headache, dizziness, rash, itch, vomiting, diarrhea, abdominal pain, chest pain, palpitations, respiratory symptoms, and weight loss. 50.0% of the patients received oral corticosteroids (OCS) and 44.2% received chronic OCS dose (>=5 mg/day prednisone equivalent).

Conclusions: Our findings highlight a substantial burden of illness and considerable unmet need in HES patients, emphasizing the need to improve diagnosis and management in this patient population.

Funded by: GSK [217426]

F22

Patient Profiles in Eosinophilic Granulomatosis with Polyangiitis (EGPA) - Insights from Allergy Practice

Michael E. Wechsler, Anna Kovalszki, Jared Silver, Brian Stone, William A. McCann, Lynn Huynh, Anamika Khanal, Mingchen Ye, Mei Sheng Duh, Arijita Deb

Rationale: The patient profile and treatment pattern for EGPA in the real-world setting are poorly understood because of the condition's rarity and lack of recognition. We performed a retrospective chart review to characterize demographics, clinical characteristics, and symptoms of patients with EGPA managed within the US Allergy Partners (AP).

Methods: Patients with EGPA were identified in the AP network EMR (2007–2021) based on a clinical diagnosis of EGPA and confirmation through lab and histopathology. Patients were followed longitudinally from index date (first AP visit) until the end of data availability.

Results: Of the 94 EGPA patients identified, 52 patients met all eligibility criteria (female:63.5%, white:57.7%, median age of EGPA diagnosis:52.5 years, median age at index:56.0 years). 3 out of every 4 patients received their first EGPA diagnosis outside the AP network and primary care physicians (50.0%) were the most commonly referring physician, followed by pulmonologist (21.2%). Most patients had asthma (92.3%) followed by rhinitis (75.0%), sinusitis (61.5%). The median of the peak absolute eosinophil count (AEC) was 700/µL. Most patients reported >=17 distinct symptoms reported during entire study period and the most frequently occurring symptoms included fatigue, headache, dizziness, rash, itch, vomiting, diarrhea, chest pain, palpitations, respiratory symptoms, and weight loss. Majority of the patients received oral corticosteroids (84.6%). Most commonly used immunosuppressive agent was azathioprine (25.0%).

Conclusions: Care of EGPA patients outside of referral centers reveals a significant disease burden featuring high comorbidity, numerous symptoms, and considerable medication usage, illustrating the need for improved diagnosis and management.

Funded by: GSK [217426]

F23

A Case Series of Live Attenuated Vaccine Administration in Dupilumab-Treated Children with Atopic Dermatitis

Elaine C. Siegfried, MD, Lara Wine Lee, PhD, Jonathan M. Spergel, MD, Sumeet Uppal, Anna Coleman, MD, Brad Shumel, MD, Randy Prescilla, MD, Ashish Bansal, MD, Sonya L. Cyr, PhD

Introduction: In patients with AD, it's unknown whether suppression of dysregulated type 2 immune cytokines with dupilumab impacts the risk of viral infections following live attenuated vaccination. Current medical consensus and regulatory labelling recommends avoiding use of live vaccines in patients treated with dupilumab. However, 9 patients in dupilumab pediatric AD clinical trials received a live attenuated vaccine.

Methods: Pediatric patients with moderate-to-severe AD who had previously participated in the phase 2 open-label, multicenter, sequential study LIBERTY AD PRESCHOOL (part A; 3 or 6mg/kg dupilumab single dose) or the randomized, double-blind placebo-controlled phase 3 study LIBERTY AD PRESCHOOL (part B; dupilumab every 4 weeks [q4w] [baseline weight 5–<15kg: 200mg; 15–<30kg: 300mg) were subsequently enrolled into the LIBERTY AD PED-OLE study (5–<15kg: 200mg dupilumab q4w; 15–<30 kg: 300mg q4w; 30–<60 kg: 200mg q2w).

Results: Nine patients with severe AD at parent study baseline were administered a live attenuated vaccine during dupilumab treatment in LIBERTY AD PRESCHOOL part B (n=1) with a ≤12-week gap between dupilumab administration and vaccination and LIBERTY AD PED-OLE (n=8), 4 patients with a ≤12-week gap and 4 patients >12 weeks since the prior dupilumab dose. Patients were first diagnosed with AD between 0–6 months of age, age at enrollment varied from 8–56 months old. Dupilumab treatment duration up to the date of vaccination with live attenuated measles, mumps, rubella (MMR) and varicella vaccines (n=5) or MMR vaccine only (n=4) ranged from 85–840 days. No adverse events (AEs), including serious AEs, or treatment-emergent infections and infestations were observed in the 4-week window post vaccination.

Conclusion: In this limited retrospective case series of children with severe AD who also received the live attenuated MMR vaccine, with or without live attenuated varicella vaccine, no major safety issues were observed after vaccination.

Funded by Sanofi and Regeneron Pharmaceuticals Inc.

F24

Patients with eosinophilic esophagitis have a high baseline burden of atopic/allergic comorbidities: from Parts A and B of LIBERTY-EoE-TREET

Marc E. Rothenberg, MD, Jonathan M. Spergel, MD, Evan S. Dellon, MD, Larry Borish, MD, Xian Sun, PhD, Kiran Patel, MD, Arsalan Shabbir, MD

Rationale: Eosinophilic esophagitis (EoE) is a chronic, progressive, type 2 inflammatory disease of the esophagus. Dupilumab, a fully human mAb, blocks the shared receptor component for interleukin (IL)-4/IL-13, key and central drivers of type 2 inflammation. In phase 3 LIBERTY-EoE-TREET (NCT03633617) dupilumab improved histologic, symptomatic, and endoscopic aspects of EoE and was well tolerated. This analysis summarizes the baseline atopic/allergic comorbidity burden of patients with EoE from Parts A and B of LIBERTY-EoE-TREET.

Methods: Baseline comorbidity data was summarized from 81 patients from Part A and 239 patients from Part B who received dupilumab or placebo.

Results: Of the 81 patients enrolled in Part A, 84% had a current history of atopic/allergic comorbid conditions; 59% had allergic rhinitis; 44% had food allergies; 48% had non-food allergies (to medication, plants, animals, mold, dust mites, etc.); 31% had asthma; 19% had atopic dermatitis; 16% had allergic conjunctivitis; 12% had contact dermatitis; 12% had hives; 10% had chronic rhinosinusitis; 1% had nasal polyps. Of the 239 patients enrolled in Part B, 89% had a current history of atopic/allergic comorbid conditions; 62% had allergic rhinitis; 54% had food allergies; 51% had non-food allergies; 38% had asthma; 20% had atopic dermatitis; 15% had allergic conjunctivitis; 16% had contact dermatitis; 18% had hives; 12% had chronic rhinosinusitis; 2% had nasal polyps.

Conclusion: A high proportion of patients in the phase 3 TREET study had atopic/allergic comorbidities. Results were consistent between Part A and B at baseline, and were aligned with previous EoE studies.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F25

Dupilumab Improves Urticaria Signs and Symptoms and Quality of Life in Patients With Chronic Spontaneous Urticaria (CSU)

Marcus Maurer, MD, Thomas B. Casale, MD, Sarbjit S. Saini, MD, Moshe Ben-Shoshan, MD, Allen Radin, MD, Deborah Bauer, MS, Ryan B. Thomas, PharmD, Leda P. Mannent, MD

Background: Chronic spontaneous urticaria (CSU) is a chronic inflammatory disease characterized by wheals and/or angioedema recurring for >6 weeks that impacts quality of life (QoL) through itch and disruptions in emotional wellbeing, daily activities, and work/school performance. Many patients continue to experience disease burden despite treatment with H1-antihistamines.

Methods: LIBERTY-CSU CUPID Study A (NCT04180488) is a randomized, placebo-controlled, phase 3 trial of dupilumab treatment for 24 weeks in adults, adolescents, and children (≥6 years) with CSU who remain symptomatic despite use of standard-of-care H1-antihistamines. Patients receiving H1-antihistamine (up to fourfold approved dose) were randomized to receive add-on dupilumab 300 mg (adults/adolescents ≥60 kg) or 200 mg (adolescents <60 kg, children ≥30 kg) (n=70) or matching placebo (n=68) subcutaneously every 2 weeks. Efficacy endpoints included the Urticaria Activity Score over 7 days (UAS7; range 0–42). Health-related QoL outcomes included the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL; range 0–100 [higher scores indicate greater QoL impairment]).

Results: Mean UAS7 and CU-Q2oL scores at baseline were 31.9/30.8 (dupilumab [n=70]/placebo [n=68]) and 41.0/46.7, respectively. UAS7 improved significantly in dupilumab-treated patients; at Week 24, least squares (LS) mean change from baseline was −20.5/−12.0 for dupilumab/placebo, respectively (difference −8.5, *P*=0.0003). Similar results were seen in CU-Q2oL scores at Week 24; LS mean change from baseline was −29.6/−21.0 for dupilumab/placebo, respectively (difference −8.6; nominal *P*=0.0049).

Conclusions: Patients with CSU treated with dupilumab experienced reduction in urticaria activity, as measured by UAS7, and improvement in quality of life, as measured by CU-Q2oL.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F26

Dupilumab Induces Clinical Remission in Patients with Uncontrolled, Moderate-to-Severe, Type 2 Inflammatory Asthma

Ian D. Pavord, MD, Elliot Israel, MD, Stanley Szefler, MD, Guy Brusselle, MD, Klaus F. Rabe, MD, Zhen Chen, PhD, Arman Altincatal, Amr Radwan, MB, Nami Pandit-Abid, Pharm D, Nikhil Amin, MD, Juby A. Jacob-Nara, MD, Paul J. Rowe, MD, Yamo Deniz, MD, Asif H. Khan, PhD, David J. Lederer, MD, William W. Busse, MD

Introduction: This analysis assesses the percentage of patients with asthma achieving clinical asthma remission with dupilumab in QUEST (NCT02414854) and TRAVERSE (NCT02134028).

Methods: Patients with uncontrolled, non-oral-corticosteroid (OCS) dependent, moderate-to-severe asthma received dupilumab 200/300 mg every 2 weeks (q2w) or matched placebo (QUEST), followed by dupilumab 300mg q2w (TRAVERSE; dupilumab / dupilumab and placebo / dupilumab groups). Clinical asthma remission was defined as: no exacerbations, no OCS use, Asthma Control Questionnaire <1.5, and improvement in pre-bronchodilator forced expiratory volume in 1 second (FEV_1) ≥100mL (TRAVERSE), or either improvement in pre-bronchodilator FEV_1 ≥100mL or post-bronchodilator percent predicted FEV_1 ≥80% (QUEST).

Results: 1584 patients from QUEST (dupilumab: n=1040/ placebo: n=544) and 1279 patients from QUEST who enrolled in TRAVERSE (dupilumab / dupilumab: n=842; placebo/ dupilumab: n=437) were included. At Year (Y) 1, 35.0% of patients treated with dupilumab met all criteria for remission, vs 20.4% with placebo. At Y1.5/2, 38.4%/36.1% of dupilumab -treated patients met all 4 criteria. 90.1% of patients met at least 1 criterion for clinical remission after 1 year of dupilumab treatment, and this effect persisted through the second year of dupilumab treatment. Clinical asthma remission was sustained under dupilumab treatment, as 70.2% of patients who met all 4 criteria at Y1 continued to meet them at Y2.

Conclusions: 35.0% of patients in QUEST achieved clinical asthma remission after 1 year of dupilumab treatment, and this was sustained in 70.2% of these patients at Y2. After an additional year of treatment in TRAVERSE, 36.1% achieved clinical remission.

Funded by Sanofi and Regeneron Pharmaceuticals Inc

F27

Preferences of People with Hereditary Angioedema for On-Demand Treatment: A US-Based Qualitative Study

Don Bukstein, Vibha Desai, Ledia Goga, Michelle Brown, Russell Settipane

Introduction: Hereditary angioedema (HAE) is a rare genetic disorder characterized by unpredictable and often debilitating subcutaneous or submucosal swelling attacks. All currently approved HAE on-demand treatments require parenteral administration, thereby increasing the burden on patients. This qualitative study assessed patient preferences (including likes/dislikes) associated with on-demand treatment.

Methods: The US Hereditary Angioedema Association (HAEA) recruited 20 people with type 1/2 HAE, who had at least one attack within previous six months and currently using on-demand treatment with or without long-term prophylaxis (LTP). Participants were interviewed about the likes and dislikes of their current on-demand treatment (open-ended questions) and efficacy/tolerability trade-offs between hypothetical self-administered parenteral and oral on-demand treatments.

Results: Ten adolescents (mean age 15.5yrs, 50% female, 80% on LTP) and 10 adults (mean age 36.7yrs, 60% female, 50% on LTP) with HAE participated. Most recent HAE attacks were treated primarily with on-demand icatibant (80%) by adults and IV pdC1-INH/rhC1-INH (60%) by adolescents. Overall, 65% liked the effectiveness of current on-demand treatment (50% adolescents/80% adults), 35% disliked injection-site pain/burning (40% adolescents/30% adults), and 25% disliked delayed response and administration burden (20% adolescents/30% adults). When presented with hypothetical parenteral and oral on-demand treatments with similar efficacy and tolerability, all participants preferred the oral treatment. Only if much better efficacy could be demonstrated within the same timeframe would a hypothetical parenteral treatment be preferred over an oral treatment by most participants (85% [90% adolescents/80% adults]). Additionally, 75% [80% adolescents/70% adults]) responded that their preference would only change from oral to parenteral treatment if tolerability/mild side-effect risk was ≥50% with the oral treatment.

Conclusions: Results highlight preference sensitive decisions involved in HAE therapy. Effectiveness and injection-site pain or burning were commonly reported likes and dislikes of current on-demand treatment, respectively. All participants preferred oral over parenteral on-demand treatment when efficacy/tolerability of the hypothetical treatments were similar.

Funded by KalVista Pharmaceuticals

F28

Sebetralstat effectiveness in the treatment of hereditary angioedema attacks rated mild or moderate at baseline in the phase 2 trial

Hilary J. Longhurst, Michael D. Smith, Christopher Yea, Paul Audhya

Introduction: Sebetralstat is an investigational oral plasma kallikrein inhibitor for on-demand treatment of hereditary angioedema (HAE) attacks. A phase 2 trial (NCT04208412) evaluated pharmacokinetics, pharmacodynamics, safety, and efficacy of sebetralstat for treatment of HAE attacks. This post hoc analysis reports effects of sebetralstat on symptom relief or improvement analyzed by baseline attack severity.

Methods: Adults with HAE type I or II with 3 or more attacks in the past 93 days participated in a randomized, double-blind, placebo-controlled, phase 2 crossover trial. Attacks were categorized as mild or moderate severity at baseline. Symptom relief was defined as a rating of at least “A Little Better” for 2 consecutive timepoints on Patient Global Impression of Change (PGI-C) or at least 50% reduction from baseline for 3 consecutive timepoints on composite visual analog scale (VAS) scores within 12 hours of study drug. Severity improvement was defined as at least 1 level reduction on Patient Global Impression of Severity (PGI-S) within 12 hours.

Results: Sixty patients completed at least 1 attack treatment (n=113 attacks). Within 12 hours of sebetralstat administration, symptom relief assessed by PGI-C was achieved for 69.2% and 89.3% of mild and moderate attacks vs 41.9% and 60.9% on placebo (difference vs placebo for mild and moderate attacks: 27.3% and 28.4%). Assessment by VAS achieved symptom relief after sebetralstat for 65.4% and 64.3% of mild and moderate attacks vs 22.6% and 43.5% on placebo (difference vs placebo for mild and moderate attacks: 42.8% and 20.8%). Severity improvement by PGI-S following sebetralstat was achieved for 34.6% and 78.6% of mild and moderate attacks vs 9.7% and 52.2% on placebo (difference vs placebo for mild and moderate attacks: 24.9% and 26.4%).

Conclusions: These results demonstrate that sebetralstat provides relief of mild and moderate HAE attacks, showing similar treatment effect regardless of baseline attack severity.

Funded by KalVista Pharmaceuticals

F29

Reporting of Administration Site Reactions with Parenteral Drugs for the On-Demand Treatment of Hereditary Angioedema Attacks – Analysis of the FAERS Database 2009 to 2022

Raffi Tachdjian, Sinisa Savic, Moshe Fridman, Joao Frade, and Paul K. Audhya

Introduction: Hereditary angioedema (HAE) is characterized by recurrent and unpredictable episodes of subcutaneous or submucosal swelling. This study examined administration site adverse drug reactions (AS-ADRs) associated with approved on-demand HAE therapies using real-world data provided by the FDA's Adverse Event Reporting System (FAERS).

Methods: We searched the FAERS database (10/01/2009-03/31/2022) for reports of all FDA-approved on-demand therapies for HAE attacks (human C1-inhibitor (pdC1-INH), ecallantide, icatibant, and recombinant C1-inhibitor (rhC1-INH)). The number of ADRs where the drug was listed as the "primary suspect" was recorded. ADR preferred terms were grouped into 15 ADR domains, and each drug's reports were calculated per year from their approval through March 2022. Descriptive results are presented. In addition, the preferred terms associated with AS-ADRs denoted on US package inserts were examined. For each drug-ADR pair, the reporting odds ratio (ROR) [two-sided 95% confidence interval] and the empirical Bayesian geometric mean (EBGM) [one-sided 95% lower bound] were calculated to detect pairs with higher-than-expected rates compared to other non-HAE parental drugs. Significance was declared when both lower 95% confidence interval bounds were >1 (Bate & Evans, 2009).

Results: The three most frequently reported AS-ADR domains were injection site pain, site swelling, and site erythema. Icatibant had highest reported rates overall and pdC1-INH had the highest rate of incorrect route of product administration and showed statistically a significant elevated risk of injection site reactions (ROR=3.59 [2.36-5.46]; EBGM=1.97 [1.39]). A trend toward increased risk of administration site reactions was found for icatibant (ROR=1.15 [1.01-1.30]; EBGM=1.00 [0.90]) and rhC1-INH (ROR=2.85 [1.82-4.48]; EBGM=1.32 [0.90]).

Conclusions: FAERS real-world data suggest that currently approved parenteral, on-demand therapies for HAE attacks are associated with AS-ADRs. These real-world descriptive results suggest that patients reported a significant treatment burden associated with FDA-approved parenteral ondemand therapies for HAE attacks.

Funded by KalVista Pharmaceuticals

F30

Exhalation Delivery System with Fluticasone (EDS-FLU) Significantly Reduces Acute Exacerbations and Associated Antibiotic Use in Chronic Rhinosinusitis

Maeve O'Connor, MD and the ReOpen Steering Committee.

Background: Chronic rhinosinusitis (CRS) is among the top reasons for adult outpatient antibiotic use; of ≈10 million office visits per year for CRS, ≈70% result in antibiotic prescription. Acute exacerbations of CRS (AECRS) are common and drive antibiotic use. No drugs have been shown effective for reducing AECRS. ReOpen1 and 2 are randomized controlled trials that evaluated prevention of AECRS with the exhalation delivery system with fluticasone (EDS-FLU; XHANCE®), a novel device delivering topical steroid into chronically inflamed sinonasal regions not typically accessible with standard nasal sprays (eg, past the nasal valve and above the inferior turbinate).

Methods: CRS patients were randomized to EDS-FLU 186µg or 372µg or placebo twice daily for 24 weeks. Frequency of AECRS, defined as worsening of at least 1 cardinal symptom of CRS (nasal congestion/obstruction, rhinorrhea, facial pain/pressure, hyposmia/anosmia) for ≥3 days requiring escalation of medical care (eg, doctor visit, antibiotic or steroid prescription), was analyzed using pooled data from both trials.

Results: Among 555 patients enrolled, 39.4% were using standard nasal steroids at study entry and 38.8% reported prior sinus surgery. There were 76 AECRS over 24 weeks, almost all (71) resulting in antibiotic use. Patients receiving EDS-FLU had significant reduction in AECRS versus placebo (incidence rate ratio [IRR]=0.39, P=0.001, vs placebo). Reduction was greater with EDS-FLU 372µg than EDS-FLU 186µg: IRR=0.34, P=0.002; IRR=0.44, P=0.012, respectively. 9.9% of patients receiving EDS-FLU 186µg and 7.8% of patients receiving EDS-FLU 372µg had ≥1 AECRS (20 and 15 events, respectively) vs 15.7% receiving placebo (41 events; P=0.012 and P=0.002 vs placebo, respectively). Reported adverse events were similar to those reported with standard-delivery nasal sprays.

Conclusions: EDS-FLU is the first medication shown in randomized controlled trials to significantly reduce acute exacerbations of CRS, offering potential to improve antibiotic stewardship by reducing a common driver of outpatient antibiotic use.

Funded by OptiNose, Inc.

F31

Lebrikizumab Decreases Inflammatory Biomarkers in Patients with Asthma: Data from Randomized Phase 3 Trials (LAVOLTA I and II)

Stanley J. Szefler, MD; Jonathan Corren, MD; Jonathan I. Silverberg, MD; Angela Okragly, MS; Zhe Sun, PhD; Chitra R. Natalie, MD; Ralph Zitnik, MD; Kimberly Siu, MD; Andrew Blauvelt, MD; Kristin Fiumara, Pharm.D.

Introduction: Lebrikizumab (LEB) was studied for treating immune mediated disorders, including asthma and atopic dermatitis. LAVOLTA I (NCT01867125) and II (NCT01868061) (LI&LII) were duplicate randomized, placebo-controlled Phase 3 LEB trials in uncontrolled asthma that enrolled subjects irrespective of asthma exacerbation history, baseline blood eosinophilia, or FeNO. LI&II failed to show consistently significant results in asthma exacerbation rate reduction. Here, effects of LEB on inflammatory biomarkers were assessed in patients with asthma.

Methods: Serum samples were tested using immunoassays for periostin (IL-13 activation marker), CCL13 (driver of chemotaxis in immune cells), CCL17 (driver of chemotaxis in Th2 cells), and IgE (hallmark of allergic inflammation). Mean changes from baseline in these markers are reported and change from baseline comparisons were evaluated using MMRM with different contrasts. Within-biomarker multiplicity controls were performed.

Results: In LI, for 125mg LEB Q4W (N=359) vs placebo Q4W (N=362) at week 1, reductions from baseline were -35.6 vs -1.7 pg/mL for CCL13; -59.3 vs -4.6 pg/mL for CCL17; and -5.3 vs -1.2 ng/mL for periostin; and week 12 reductions from baseline were -49.5 vs -8.8 IU/mL for IgE. Differences with 125mg LEB Q4W were significant ($p < 0.0001$), differences with placebo were not. Similar reductions were seen for LEB 37.5mg Q4W and for LII. Reductions were maintained during the 52-week LI&LII treatment periods.

Conclusions: LEB treatment decreased inflammatory biomarkers in asthma. Reductions in circulating inflammatory biomarkers were observed as early as 1 week following a single LEB dose. Improvements in inflammation were maintained during 52 weeks of LEB treatment.

Funded by Eli Lilly and Company

F32

Efficacy of Lebrikizumab in Patients with Atopic Dermatitis and Atopic Comorbidities: Pooled Results from 2 Phase 3 Monotherapy Randomized, Double-Blind, Placebo-Controlled 16-Week Studies (ADvocate1 and ADvocate2)

Ellen R. Sher, MD; Mark Boguniewicz, MD; Alexandra K. Golant, MD; Marjolein de Bruin-Weller, PhD; Jose-Manuel Carrascosa, PhD; Jinglin Zhong, MS; Zach Dawson, PhD; Amber Reck Atwater, MD; Kimberly Siu, MD; Jacob P. Thyssen, PhD; Kristin Fiumara, Pharm.D.

Introduction: Atopic comorbidities are common in patients with atopic dermatitis (AD). We evaluated lebrikizumab, a high-affinity monoclonal antibody targeting interleukin-13, in patients with AD with and without atopic comorbidities in 2 Phase 3, randomized, double-blind trials (ADvocate1 [NCT04146363] and ADvocate2 [NCT04178967]).

Methods: Adults and adolescents with moderate-to-severe AD were randomized 2:1 to subcutaneous lebrikizumab 250 mg (N=564) or placebo (N=287) every 2 weeks. Using pooled data, treatment comparisons in patients with and without atopic comorbidities were assessed at Week 16 by percentage of patients achieving Investigator's Global Assessment (IGA) (0,1) with ≥2-point improvement, Eczema Area and Severity Index 75% improvement (EASI75), and Pruritis Numeric Rating Scale (PNRS) ≥4-point improvement (in patients with baseline PNRS ≥4).

Results: Of 851 patients, 614 (72.2%) reported ≥1 atopic comorbidity (1 [n=54], 2 [n=200], 3 [n=131], or >3 [n=229] atopic comorbidities), most commonly allergic rhinitis (49.6%), food allergy (32.1%), and asthma/asthma history (30.7%). At Week 16 among patients with ≥1 atopic comorbidity, more lebrikizumab- vs. placebo-treated patients reported IGA (0,1) with ≥2-point improvement (36.7% vs. 12.0%; $p<0.001$), EASI75 (55.6% vs. 16.7%; $p<0.001$), and PNRS ≥4-point improvement (42.2% vs. 10.1%; $p<0.001$). Similarly, among patients without atopic comorbidities, more lebrikizumab- vs. placebo-treated patients reported IGA (0,1) with ≥2-point improvement (41.8% vs. 11.1%; $p<0.001$), EASI75 (55.2% vs. 18.5%; $p<0.001$), and PNRS ≥4-point improvement (45.0% vs. 17.6%; $p<0.001$) at Week 16.

Conclusions: Lebrikizumab provided clinically meaningful improvements in skin and itch in patients with moderate-to-severe AD, regardless of coexisting atopic comorbidities.

Funded by Eli Lilly and Company

Eastern Allergy Conference
June 1-4, 2023 ~ Palm Beach, FL

Scientific Posters S1-S32 will be on display in the Ponce Foyer during the coffee break, 10:00 – 11:00am, Saturday June 3, 2023

Not for CME Credit

S1

Bird fanciers' disease in a pigeon breeder

Bijalben Patel, MD, Walaa Hamadi, MD

Introduction: Hypersensitivity pneumonitis (HP) results from an abnormal immune response caused by repeated inhalation of various antigens in susceptible and sensitized individuals. HP is induced by numerous agents and can escape detection or be misdiagnosed.

Case Report: A 74-year-old male was referred to us with a dry cough for over 3 years associated with shortness of breath. His past medical history is significant for rheumatoid arthritis (RA)- well controlled on sulfasalazine, mild persistent asthma, and allergic rhinitis. On examination, he had fine bibasilar crackles otherwise unremarkable. Pulmonary function test showed FVC: 100%, FEV1: 87%, FEV1/FVC of 66%, and DLCO at 114%. High resolution computed tomography (HRCT) of the chest showed mild honeycombing, traction bronchiectasis, and bilateral subpleural interstitial septal thickening. Pulmonary team evaluated patient and did not suspect RA associated interstitial lung disease (ILD). Social history revealed that he is breeding around 70 pigeons. Laboratory evaluation revealed an elevated absolute eosinophil count of 570, elevated IgE of 3155, and a positive serum pigeon IgG. Patient was diagnosed with HP and counseled to remove all birds from his home.

Discussion: The clinical presentation of HP can be acute, subacute, or chronic. Chronic HP manifests as dyspnea and cough. Lung function shows restriction with reduced gas transfer. HRCT findings include fibrosis, reticular pattern, honeycombing, and traction bronchiectasis which are difficult to distinguish from other forms of ILD. In a patient with a history of exposure to a known offending antigen, a confident diagnosis of HP can be made when HRCT shows classic features and serology is positive for antigen-specific IgG. This case highlights the importance of gathering a thorough history. Given the patient's history of RA, his symptoms could have mistakenly been related to RA-associated ILD. Prompt evaluation for suspected HP can ultimately prevent the progression of pulmonary disease via antigen avoidance.

S2

Trends in Anaphylaxis

Walaa Hamadi, MD, Thomas Casale, MD

Rationale: The purpose of this study is to identify trends in anaphylaxis epidemiology and clinical implications to further guide management of acute at home and in Emergency Room (ER) anaphylactic events.

Methods: Data collected from a survey sent to individuals in the FARE Patient Registry and a retrospective review of electronic medical records of patients who presented to Tampa General Hospital ER for anaphylaxis based on ICD10code and treatment received (epinephrine).

Results: We received 190 FARE survey responses of patients that had an allergic reaction during COVID (3/2020-1/2022). Triggering allergens included peanut (14%), tree nuts (18%), egg (10%), milk (8%), seafood (10%), wheat (7%), soy (3%) and sesame (3%). Less than 2% of reactions occurred at a doctor's office. 63 (33%) patients reported that the COVID-19 pandemic changed how they responded to the allergic reaction: 71% avoided seeking medical care outside the home, 30% used medication more quickly than normal, and 14% delayed use of medication. Only 87 patients (46%) were treated with epinephrine. 4,358 patients presented to TGH ER from April 1, 2018 to March 31, 2022 with a diagnosis of anaphylaxis or acute allergic reaction. Only 718 (16%) received epinephrine in the ER. The most frequently used ICD-10 code for those who received epinephrine was 'allergy to other food'. Females presented twice as much as males. 867 patients presented 1 year prior to March 1, 2020 and 1,833 patients presented 1 year after April 1, 2021 (pre- and post-covid vaccine availability).

Conclusions: Food remains the major trigger for anaphylaxis. Covid did not appear to discourage ER visits for treatment. Only 16% and 46% of patients received epinephrine in the ER groups and survey, respectively. There continues to be hesitancy to use epinephrine by both the patient (survey data) and in the ER, which can lead to greater adverse consequences.

S3

Worsening hypereosinophilia with use of dupilumab

Sonia Mathew, MD; Timothy Kubal, MD, MBA; Farnaz Tabatabaian, MD

Introduction: Dupilumab has proven clinical success in multiple atopic diseases. Dupilumab is known to be associated with a transient eosinophilia that typically declines over time and is rarely of clinical significance. However, a small number of case reports report worsening eosinophilia with clinical manifestations in patients taking dupilumab. We report a patient who had worsening eosinophilia with the use of dupilumab and was eventually diagnosed with Hypereosinophilic Syndrome (HES).

Case Presentation: A 28-year-old female presented with 4-year duration of dyspnea with minimal exertion, chest tightness, and nocturnal coughing. Her symptoms did not respond to asthma treatments including ICS/LABA/LAMA combination therapy. Symptoms improved only with oral glucocorticoids, requiring daily prednisone approximately 2-3 weeks/month. She was treated with dupilumab from May 2021 to July 2021 without improvement in symptoms. Dupilumab was stopped due to hypereosinophilia with absolute eosinophil count (AEC) of 6000 cells/microliter, increased from 1670 cells/microliter before starting dupilumab. She had no history of frequent infections to suggest immunodeficiency. Physical exam was unremarkable, but she provided pictures of her skin prior to prednisone which showed large erythematous plaques with red borders and central clearing in her groin and abdomen. Further laboratory work-up revealed negative c-KIT mutation, normal tryptase, immunoglobulins, TSH, C1q, C3, C4, ESR, and CRP as well as a negative autoimmune panel, c-ANCA, p-ANCA, RF, HIV, and HCV antibody testing. Bone marrow biopsy revealed normocellular marrow and 14% eosinophils; immunohistochemical staining for CD34 and CD117 showed 2% blasts and scattered mast cells without increase in spindle shaped mast cells or dense mast cell clustering. Genetic testing and T cell studies were unremarkable. The patient was diagnosed with idiopathic HES and is being treated with mepolizumab every 4 weeks. Her AEC reduced to 40 cells/microliter but respiratory symptoms still require prednisone from time to time.

Discussion: This case highlights the need for clinicians to be aware of the potential for eosinophilic complications or even unmasking of disease in patients on dupilumab. Patients should be monitored regularly for changes in eosinophilia and imaging should be obtained promptly if respiratory symptoms suddenly worsen. Given the short course of dupilumab, it is likely that treatment unmasked HES and was not causative.

S4

A Dash of Danger: A Rare Case of Paprika Anaphylaxis

A.T. Nguyen, W. Bao, V. Nguyen, R.A. Settipane

Introduction: Anaphylaxis due to spices is rare. Case reports have described anaphylaxis with thyme, cumin, and oregano. However, there have only been a few cases of paprika food allergy published. Diagnosing a paprika allergy may be challenging due to the infrequency of true anaphylaxis to the spice and the common practice of adding many spices into a single dish.

Case Description: A 18 year-old female was referred for allergic evaluation after she developed post-prandial acute swelling of her lips, generalized pruritis and hives requiring an emergency room visit and treatment with epinephrine. Symptoms developed 45-60 minutes after eating a restaurant meal consisting of traditional Indian foods including chicken marsala and chickpeas. She was evaluated by her primary care provider by serum IgE to a random panel of numerous foods, all of which were negative. At the time of referral for allergy consultation, she was instructed to obtain an extensive ingredient list from the restaurant. The list included over one dozen different foods and spices. Skin prick testing was negative to soy, rice, corn, and mustard. Serum IgE testing was negative to chickpea, soy, cilantro, cumin seed, fenugreek seed, mango, and mustard, but positive to paprika. This spice was deemed the likely cause of her food anaphylaxis. She was advised to strictly avoid paprika, given an anaphylaxis treatment plan, and prescribed/trained on an epinephrine autoinjector.

Discussion: This case demonstrates anaphylaxis due to paprika which is uncommonly reported in the literature. This case also illustrates the importance of obtaining a thorough history and performing targeted food allergy testing. Although paprika anaphylaxis is rare with a single case report listed in the literature, recognition of paprika food allergy is critical for the prevention of future episodes of anaphylaxis and potential associated risks of morbidities and mortality.

S5

Dupilumab Improves Chronic Rhinosinusitis With Nasal Polyps Disease Outcomes Irrespective Of Type 2 Signature Definition

Claus Bachert MD, Asif H. Khan PhD, Stella E. Lee MD, Anju T. Peters MD, Scott Nash MD

Introduction Chronic rhinosinusitis with nasal polyps (CRSwNP) is a disease of the nasal cavity and paranasal sinuses characterized by type 2 (T2) inflammation. Different algorithms that identify T2 inflammation in CRSwNP have been suggested. This analysis aims to evaluate dupilumab clinical efficacy by these definitions.

Methods Efficacy was assessed by baseline T2 signature definition (1. ≥150 eosinophils/μL or total ≥IgE 100 IU/mL or any coexisting T2 condition; 2. ≥150 eosinophils/μL or total ≥IgE 100 IU/mL; 3. ≥150 eosinophils/μL; 4. ≥250 eosinophils/μL or total IgE ≥100 IU/mL; 5. asthma or ≥300 eosinophils/μL; 6. any coexisting T2 condition) by least squares (LS) mean differences (dupilumab versus placebo) in change from baseline in nasal polyps score (NPS), nasal congestion/obstruction (NC) score, and loss of smell (LoS) score at Weeks 24 and 52 in the intention-to-treat populations of SINUS-24 and SINUS-52 (NCT02912468/NCT02898454), respectively.

Results At Week 24, LS mean differences for dupilumab versus placebo by baseline T2 signatures ranged from −2.32 to −2.14 for NPS, −1.10 to −0.92 for NC, and −1.20 to −1.07 for LoS (all $P < 0.0001$). Similar results were observed at Week 52: −2.64 to −2.40 for NPS, −1.12 to −1.01 for NC, and −1.28 to −1.12 for LoS (all $P < 0.0001$).

Conclusion Dupilumab demonstrated robust efficacy across all definitions (combinations and permutations) of T2 inflammation consistent with its profile as an inhibitor of IL-4 and IL-13 signaling, key and central drivers of type 2 inflammation in CRSwNP.

Funded by Sanofi/Regeneron

S6

Association between Smell Loss, Disease Burden, and Dupilumab Efficacy in Chronic Rhinosinusitis with Nasal Polyps

Zach Soler MD, Andrew P. Lane MD, Zara M. Patel MD, Jose L. Mattos MD

Introduction: This post-hoc analysis investigated the association between baseline smell loss and other aspects of disease in chronic rhinosinusitis with nasal polyps (CRSwNP), and evaluated the effects of dupilumab according to severity of baseline smell loss in the pooled SINUS-24 and SINUS-52 studies (NCT02912468, NCT02898454).

Methods: Nasal polyp score (NPS, 0−8), patient-reported nasal congestion/obstruction (NC, 0−3), and 22-Item Sinonasal Outcome Test (SNOT-22, 0−110) were analyzed according to baseline weekly average patient-reported loss of smell scores (LoS, 0−3) of >1−≤2 (moderate) or >2−≤3 (severe) in patients randomized to dupilumab 300 mg or placebo every 2 weeks.

Results: A total of 724 patients were randomized. Baseline LoS was severe in 601 patients (83%) and moderate in 106 patients (15%). At baseline, odds ratios (95% CI) for severe vs moderate LoS were 1.12 (0.96, 1.32) with 1-point increase in NPS, 6.01 (3.95, 9.15) with 1-point increase in NC, 1.03 (1.02, 1.05) with 1-point increase in SNOT-22, and 3.01 (1.97, 4.59) for with vs without prior sinonasal surgery. At Week 24, least squares mean differences (95% CI) dupilumab vs placebo in change from baseline were: NPS −1.90 (−2.56, −1.25) and −1.95 (−2.20, −1.70) in the moderate and severe baseline LoS subgroups, respectively; NC −0.35 (−0.64, −0.06) and −1.00 (−1.13, −0.87); and SNOT-22 −7.52 (−14.55, −0.48) and −21.72 (−24.63, −18.82); all nominal P <0.05 vs placebo.

Conclusion: More severe smell loss is associated with greater disease burden in CRSwNP. Dupilumab significantly improved outcomes and HRQoL regardless of baseline severity of smell loss.

Funded by Sanofi/Regeneron

S7

Efficacy and Safety of Avapritinib in Indolent Systemic Mastocytosis (ISM): Results From the Double Blinded Placebo-Controlled PIONEER Study

Mariana Castells, MD, PhD, Jason Gotlib, MD, Matthew Giannetti, MD, Ilda Bidollari MD, MBA,, Hui-Min Lin, PhD,, Robyn Scherber, MD, Maria Roche, MS, Cem Akin, MD, PhD, and Marcus Maurer, MD

Introduction: ISM, a clonal mast-cell disease primarily driven by the *KIT* D816V mutation, can cause life-long debilitating symptoms. PIONEER (NCT03731260) assessed efficacy and safety of avapritinib, a potent, highly selective KIT D816V inhibitor, *vs* placebo, both with best supportive care (BSC).

Methods: Patients with moderate to severe ISM (total symptom score [TSS] ≥28) were randomized 2:1 to once-daily 25 mg avapritinib (n=141) or placebo (n=71), both with BSC. The primary endpoint was mean change in TSS (range 0–110), based on 14-day average of patient-reported severity of 11 ISM symptoms (0=none; 10=worst imaginable). Secondary endpoints included change in biomarkers of mast-cell burden (≥50% reduction in serum tryptase, bone marrow mast-cell burden, and *KIT* D816V variant allele fraction); change in most severe symptom and skin domain on the ISM-Symptom Assessment Form (©2018 Blueprint Medicines Corporation); and quality of life (QoL; assessed using the MC-QoL [a validated questionnaire] with total scores of >60 [severe], 40–60 [moderate], and 20–40 [mild]). Safety was also assessed. One-sided *P*-values are reported.

Results: Avapritinib treatment *vs* placebo significantly improved TSS at 24 weeks (–15.6 *vs* –9.2; *P*=0.003), reduced objective measures of mast-cell burden (all *P*<0.0001), and reduced most severe symptom score (mean change [SD] –2.2 [2.3] *vs* –1.4 [1.9]; *P*=0.015). In patients with skin disease, mean (SD) change in skin domain was greater with avapritinib (n=107; −7.2 [6.4]) *vs* placebo (n=60; −2.8 [4.2]); *P*<0.0001. Improvement in MC-QoL mean total score (SD) from baseline to Week 24 was greater with avapritinib (57.5 [16.0] to 38.1 [21.6]) *vs* placebo (57.5 [17.2] to 47.1 [20.9]). Avapritinib was well-tolerated, with a safety profile comparable to placebo.

Conclusions: Avapritinib treatment was safe and well-tolerated, and markedly improved mast-cell burden, symptoms, and QoL, potentially offering a promising new treatment option for ISM.

Funded by Blueprint Medicines Corporation.

S8

The Asthma Impairment and Risk Questionnaire (AIRQ®) Predicts Short- and Long-term Risk of Exacerbations in Adolescents and Adults with Asthma

William McCann, Bradley Chipps, David A. Beuther, Robert S. Zeiger, Robert A. Wise, Joan Reibman, Maureen George, Ileen Gilbert, James M. Eudicone, Hitesh N. Gandhi, Gale Harding, Katelyn Cutts, Kevin R. Murphy

Introduction: The Asthma Impairment and Risk Questionnaire (AIRQ®) is a 10-item, yes/no, control tool: 0-1 yes responses indicate well-controlled (WC); 2-4 not well-controlled (NWC); 5-10 very poorly controlled (VPC). AIRQ® predicts exacerbations within the next 12 months. This study examines the ability of AIRQ® to predict exacerbations within a short-term (0-3 months) and long-term (4-12 months) time frame.

Methods: Patients aged ≥12 years completed a baseline AIRQ® and 12 monthly online reports of exacerbations (asthma-related oral corticosteroid courses, emergency department/urgent care visits, and hospitalizations). Logistic regressions using AIRQ® control level as the independent variable, with age, sex, race, and BMI as covariates, and ≥1 exacerbation within months 0-3 and months 4-12 as the dependent variable (adjusted odds-ratios [OR] and 95% Wald confidence intervals [CI]) were performed.

Results: 1070 patients completed ≥1 survey (mean[SD]: 10.5[2.8] surveys; 70.5% female; age 43.9[19.3] years; 20.4% non-White; AIRQ® WC 35.2%, NWC 38.1%, VPC 26.6%). Within months 0-3 and 4-12, 277 and 376 patients, respectively, experienced ≥1 exacerbation. Exacerbation rates, whether within the short- or long-term, increased with worsening AIRQ® control (0-3 months: 13.8% WC, 26.0% NWC, 45.4% VPC; NWC vs WC: OR=2.17 [CI: 1.49, 3.15], VPC vs WC: OR=4.51 [CI: 3.05, 6.67]; 4-12 months: 20.7% WC, 38.4% NWC, 53.5% VPC; NWC vs WC: OR=2.37 [CI: 1.70, 3.30], VPC vs WC: OR=3.83 [CI: 2.67, 5.48]). No significant difference in AIRQ® exacerbation prediction performance between time periods was observed.

Conclusions: AIRQ® predicts short- and long-term exacerbations and can heighten awareness of potential imminent and distant exacerbation risk.

Funded by AstraZeneca

S9

Machine-learning Model Identifies Patients Across the United States Who Have a High Probability of Alpha-1 Antitrypsin Deficiency

Jimmy Hinson, Richard Colbaugh, Kristin Glass, Iris Himmelhan, Marie Sanchirico

Introduction: Alpha-1 antitrypsin deficiency (AATD) is a genetic condition that can cause severe lung disease in adults and has symptoms similar to common lung diseases. Lack of AATD screening has resulted in >90% of patients with AATD-associated genotypes in the United States (US) remaining undiagnosed. We developed a machine-learning model to identify undiagnosed, symptomatic patients with high predicted-probability of AATD (hPP-AATD) using administrative claims data.

Methods: Using data from >150 million deidentified patient records (January 1, 2016–April 1, 2021; available from the Komodo Health US healthcare claims database), 5 patient cohorts were created to train and assess predictive models. Model predictions were validated using expert opinions from clinicians. Models identified likely-diagnosed (with AATD diagnosis, medication prescriptions, or diagnostic test claims in patient records) and likely-undiagnosed patients (with hPP-AATD but no evidence of AATD diagnosis).

Results: Our model identified ~47,000 likely-diagnosed and ~141,000 likely-undiagnosed patients with AATD, and found the estimated US prevalence of AATD to be ~1/2900. West Virginia, Kentucky, and South Dakota had the maximum likely-diagnosed patients with AATD per 100,000 people. Over half of the likely-undiagnosed, symptomatic patients with hPP-AATD were found in 10 states including California, Texas, and Florida. AATD likelihood (diagnosed and undiagnosed) correlated directly with rural population percentage and prevalence of smoking and liver-disease-related deaths, and inversely with median income. Most symptomatic patients with hPP-AATD were 60–70 years old.

Conclusions: Our model identified many likely-undiagnosed, symptomatic patients with hPP-AATD in the US, suggesting that symptomatic patients are often unaware of their genetic susceptibility for AATD-related lung/liver disease. Timely identification of symptomatic patients can help diagnose at-risk, presymptomatic family members and enable lifestyle modifications, access to augmentation therapy, and/or other care specific to their genetic predisposition to AATD to prevent or delay disease severity.

Funded by Takeda Pharmaceuticals USA, Inc.

S10

Efficacy and safety of hyaluronidase-facilitated subcutaneous immunoglobulin 10% in US pediatric patients with primary immunodeficiency disease

Niraj C. Patel, Jolan E. Walter, Richard L. Wasserman, Arye Rubinstein, T. Prescott Atkinson, Meagan W. Shepherd, Erin Greco, Sharon Russo-Schwarzbaum, Kimberly Duff, Barbara McCoy, Liang-Hui Chu, Zhaoyang Li, Leman Yel

Introduction: This study assessed efficacy and safety of facilitated subcutaneous immunoglobulin (fSCIG; immunoglobulin G [IgG] 10% and recombinant human hyaluronidase [rHuPH20]) in US pediatric patients with primary immunodeficiency disease (PIDD), also known as inborn errors of immunity (IEI).

Methods: This phase 3, open-label, prospective study (NCT03277313) was conducted at 17 US centers. Eligible patients were aged 2 to <16 years, diagnosed with PIDD/IEI requiring immunoglobulin replacement therapy, and received a consistent IgG dose for ≥3 months before screening. Patients received fSCIG 10% using a dose ramp-up over ≤6 weeks (Epoch 1) followed by fSCIG 10% treatment every 3 or 4 weeks for ≤3 years (Epoch 2). The primary endpoint, rate of acute serious bacterial infections (ASBIs), was compared to the regulatory-defined threshold (<1.0 ASBIs/patient-year).

Results: 44 Epoch 1 patients (mean age [range] 9.0 [3–15] years, 59.1% male) and 43 Epoch 2 patients provided final data; 34 patients completed the study. Two ASBIs (bacterial pneumonia) occurred in 1 patient. Mean rate of ASBIs (0.04 events/patient-year [99% upper CI:0.20]) was significantly lower than the regulatory-defined threshold. Mean rate of infections was 3.12 events/patient-year. Stable mean serum trough IgG levels were maintained during Epoch 2 (10.4, 9.2, 9.2 g/L at months 0, 6, 12, respectively). Excluding infections, 336 fSCIG-related treatment-emergent adverse events (TEAEs) occurred in 34 patients (Epochs 1/2 combined); most were mild (247 events in 32 patients) with 2 severe TEAEs in 2 patients (celiac disease flare, headache). One serious TEAE (tonsillar hypertrophy) was considered unrelated to fSCIG 10%. One patient developed anti-rHuPH20 binding antibodies (titer ≥160) without neutralizing anti-rHuPH20 antibodies. At end of Epoch 2, most patients wanted to continue fSCIG 10%.

Conclusions: fSCIG 10% effectively prevented ASBIs in US pediatric patients with PIDD/IEI with a consistent safety profile.

Funded by Takeda Pharmaceuticals USA, Inc.

S11

Efficacy of lanadelumab at fixed and modified dosing regimens in patients aged 2 to <12 years old with hereditary angioedema (HAE) in the phase 3, open-label, multicenter SPRING Study

William Lumry, Jonathan A. Bernstein, Raffi Tachdjian, H. James Wedner, William Yang, Marcus Maurer, Inmaculada Martinez-Saguer, Henriette Farkas, Christina Nurse, Ming Yu

Introduction: In the SPRING Study (NCT04070326), lanadelumab efficacy with fixed and modified dosing was evaluated in HAE patients aged 2–<12 years.

Methods: Pediatric patients with HAE-1/2 and a baseline HAE attack rate of ≥1 attack/12 weeks were enrolled. Patients aged 2–<6 years received fixed dosing of lanadelumab 150 mg every 4 weeks (Q4W) during two consecutive 26-week treatment periods (A, B). Patients aged 6–<12 years received 150 mg every 2 weeks (Q2W) during Period A and could modify to Q4W during Period B if they were attack-free for 26 weeks.

Results: In total, 21 patients were enrolled. In the 2–<6(n=4) and 6–<12(n=17) groups, mean(SD) attack rate was 1.86(1.03) and 1.84(1.65) attacks/month at baseline, respectively. At fixed dosing during Period A, attack rates decreased to 0.15(0.31) (-95.3%) and 0.08(0.21) (-93.4%), respectively; 3/4(75.0%) and 14/17(82.4%) patients, respectively, were attack-free. During Period B, 7 patients in the 6–<12 group switched to Q4W; their attack rate was maintained at 0(0) (-100%). Among the 3 patients in the 2–<6 group entering period B, 1 patient, after turning 6 years old, switched from Q4W to Q2W due to recurrent attacks; the attack rate decreased from 2.8 attacks/month (Q4W) to 0.2 (Q2W). The other 2 patients who remained on Q4W remained attack-free.

Conclusions: Efficacy was shown with both lanadelumab 150 mg Q4W and Q2W dosing in patients 2–<6 and 6–<12 years old and dosing frequency was reduced from Q2W to Q4W in patients who were attack-free for 6 months.

Funded by Takeda Development Center Americas, Inc.

S12

Patient-centric design of a multivial access device using modular innovation principles to further improve the facilitated subcutaneous immunoglobulin administration experience

Kimberly Duff, RN, Stefan Holzner, PhD, Madeleine Gibson, MSIE, Seth Jones, BSc, Thomas Amsler, BSc, Scott Ariagno, MSc

Introduction: Facilitated subcutaneous immunoglobulin 10% (fSCIG 10%), provided as a dual-vial unit (DVU) of human immunoglobulin G (IgG) 10% and recombinant human hyaluronidase (HY), is approved for treatment of adults with inborn errors of immunity (IEI) in the United States. The current fSCIG 10% infusion process involves repeating multiple steps for patients requiring multiple DVUs. We hypothesized that this process could be improved using patient-centric design and modular innovation principles.

Methods: Ethnographic research elucidated patient and nurse experiences with fSCIG 10% administration and identified infusion process improvement opportunities. Device design objectives were informed by 4 patients receiving fSCIG 10% for IEI (at-home observations and feedback sessions) and 4 nurses providing fSCIG 10% infusion training (interviews and mock training sessions): (1) simplify steps for fSCIG 10% preparation/infusion; (2) standardize equipment and infusion stages; and (3) improve patient mobility during infusions. Formative usability evaluation research with 10 patients and 4 nurses assessed prototypes of a multivial access device; observations instructed final device development.

Results: The final device (HyHub) is a tray with 4 DVU docks. Tubing under docking stations connects HY and IgG vials with color-coded connectors. HY preparation involves removing cover(s) from dock(s), inserting DVU(s), and drawing HY into a syringe from the HY connector. To prepare IgG, pump tubing is attached to the IgG connector, which cannot connect to syringes. Though administration is similar to the current method, the multivial access device improves the fSCIG 10% infusion process by simplifying preparation, reducing components, and increasing patient mobility during infusions with the device carrier.

Conclusions: Patient-centric design and modular innovation principles informed the development of a multivial access device to improve patient experiences with fSCIG 10% infusion. Further research will assess its impact on quality of life.

Funded by Takeda Pharmaceuticals USA, Inc.

S13

Remibrutinib Improves Chronic Spontaneous Urticaria in Patients Irrespective of Previous Anti-IgE Treatment: Results From a Phase 2b Study

Alexander Greiner, Sridhar Guduri, Jeffrey Leflein, Sibylle Haemmerle, Karine Lheritier, Pauline Walsh, Ivan Nikolaev, Ana Giménez-Arnau, Marcus Maurer

Objective: To explore the effect of remibrutinib (LOU064), a novel oral Bruton's tyrosine kinase (BTK) inhibitor, in patients with chronic spontaneous urticaria (CSU) with or without previous anti-IgE treatment for CSU.

Methods: In this Phase 2b study (NCT03926611), 311 patients with CSU were randomized equally to receive remibrutinib 10 mg once daily (qd) /35 mg qd /100 mg qd /10 mg twice daily (bid) /25 mg bid / 100 mg bid or placebo for 12 weeks. Outcomes included change in weekly Urticaria Activity Score (UAS7) from baseline and rate of patients achieving UAS7=0 and UAS7≤6 at Week 12, with or without previous anti-IgE treatment.

Results: At baseline, 27% (84/311) of patients had a history of previous anti-IgE treatment. At Week 12, no consistent difference in UAS7 change from baseline was observed between subgroups with or without previous anti-IgE treatment: remibrutinib 10 mg qd: −21.1 and −20.6; remibrutinib 35 mg qd: −25.2 and −19.0; remibrutinib 100 mg qd: −7.7 and −18.8; remibrutinib 10 mg bid: −14.8 and −20.5; remibrutinib 25 mg bid: −25.8 and −18.7; remibrutinib 100 mg bid: −26.2 and −18.1; and placebo: −2.8 and −9.7. Similarly, no different trends were observed in subgroups with and without previous anti-IgE treatment in terms of proportion of patients achieving UAS7=0 and UAS7≤6, across remibrutinib doses and placebo, at Week 12.

Conclusion: At all doses, remibrutinib showed improvement in UAS7 and achievement of UAS7=0 and UAS7≤6 irrespective of previous anti-IgE treatment. Larger studies are required to confirm the findings of this Phase 2b study.

Funded by Novartis Pharma AG

S14

Remibrutinib (LOU064) reduces the use of rescue medication in patients with chronic spontaneous urticaria: Findings from a Phase 2b study

Marcus Maurer, John Reed, Petra Staubach, Karine Lheritier, Pauline Walsh, Vinayak Meti, Ivan Nikolaev, Sibylle Haemmerle, Ana Giménez-Arnau

Background: Chronic spontaneous urticaria (CSU) is the spontaneous occurrence of wheals (hives) and/or angioedema for ≥6 weeks. Second-generation H_1-antihistamines (H_1-AH) are recommended as first-line treatment for CSU. Here, we report on the use of H_1-AH as rescue medication in patients with CSU in a dose-finding Phase 2b study of remibrutinib (LOU064), an oral Bruton's tyrosine kinase inhibitor.

Methods: In this multicenter, randomized, double-blind, placebo-controlled study, patients with CSU, inadequately controlled by H_1-AH (weekly Urticaria Activity Score≥16), received remibrutinib 10 mg once daily (q.d.); 35 mg q.d.; 100 mg q.d.; 10 mg twice daily (b.i.d.); 25 mg b.i.d.; 100 mg b.i.d; or placebo (1:1:1:1:1:1:1:1) for up to 12 weeks. Patients received H_1-AH at a locally approved dose as background therapy throughout the study. Rescue therapy with an alternative second-generation H_1-AH was given as needed to treat unbearable symptoms during screening, treatment, and follow-up. The number of rescue H_1-AH tablets to control itch/hives within the preceding 24 hours was recorded by patients using an eDiary. Weekly use of rescue medication was calculated as the sum of the daily dose over 7 days.

Results: In total, 311 patients were randomized to remibrutinib (10 mg q.d. [n=44], 35 mg q.d. [n=44], 100 mg q.d. [n=47], 10 mg b.i.d. [n=44], 25 mg b.i.d. [n=44], and 100 mg b.i.d. [n=45]) or placebo (n=43). Of these, 309 were included in the full analysis set. A reduction in weekly rescue medication use was observed early across all remibrutinib arms and remained low throughout the study (mean weekly range across doses: 2.8–8.2 [Weeks 1–12] vs. 6.4–9.4 [baseline]). In contrast, rescue medication use increased in the placebo group. At Week 12, the mean weekly use of rescue medication tablets was numerically lower in all remibrutinib arms compared to baseline (10 mg q.d.: 5.8 vs. 8.7; 35 mg q.d.: 3.9 vs. 6.6; 100 mg q.d: 4.0 vs. 6.4; 10 mg b.i.d: 5.1 vs. 7.6; 25 mg b.i.d.: 4.5 vs. 9.0; and 100 mg b.i.d.: 7.1 vs. 9.4); however, it was increased in the placebo group (11.9 vs. 9.0).

Conclusion: Across all doses, remibrutinib reduced the need for rescue medication at 12 weeks vs baseline and compared to placebo in patients with CSU; this was associated with improved CSU symptoms, as reported previously, despite reduced H_1-AH use.

Funded by Novartis Pharma AG

S15

Reductions in Infections and Associated Complications in Nine Common Variable Immunodeficiency Patients Treated with Immune globulin intravenous, human-slra

Jody Huss APRN-CNP, Don McNeil MD, Stephanie Melton APRN-CNP, Gordon Myers MD

Background: Common variable immunodeficiency (CVID) is a primary immune deficiency disease characterized by defects in humoral immunity. Individuals with CVID often experience frequent bacterial and viral infections of the upper airway, sinuses, and lungs despite standard immunoglobulin replacement therapy (IgRT). Immune globulin intravenous (IVIG), human-slra 10% is a unique IgRT that is manufactured from blending normal source plasma with plasma from donors that possess high antibody titers again RSV and other common respiratory pathogens.

Purpose: To evaluate the efficacy of this unique IgRT in the management of nine CVID patients.

Methods: Demographic data, medical history, and clinical course for each patient was evaluated pre- and post- initiation of IVIG human-slra.
Results: Eight patients switched from other IgRT preparations to ASCENIV™, and one patient with high-risk features (bronchiectasis, severe asthma, chronic and recurrent infections) was initiated on IVIG human-slra. All patients responded to therapy with decreased incidence of respiratory infections with over one-third of patients reporting no infections after initiating IVIG human-slra. Patients also reported reduced exacerbations of underlying asthma, better control of chronic respiratory disease, and improvement in associated complications. All patients tolerated therapy well with no serious safety events reported.

Conclusions: This case report series has demonstrated the beneficial effects of IVIG human-slra in CVID patients, providing enhanced protection against common respiratory pathogens, evidenced by decreased respiratory infections, associated complications, anti-infective utilization, and health care provider visits/hospitalizations.

Funded by ADMA

S16

Evaluating treatment responses of dupilumab versus omalizumab in severe chronic rhinosinusitis with nasal polyps and comorbid asthma patients: the EVEREST trial

De Prado Gomez L, PharmD, MSc; Khan AH, MBBS, MPH; Peters AT, MD; Bachert C, MD, PhD; Wagenmann M, MD; Heffler E, MD, PhD; Hopkins C, BMBCh; Hellings P, MD, PhD; Zhang M, PhD; Xing J, PhD; Rowe P, MD; Jacob-Nara J, MD, MPH, DHSc

Background: Dupilumab (DUP) and Omalizumab (OMZ) are approved for the treatment of uncontrolled Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) and asthma. Head-to-head comparison studies of these interventions may contribute to evidence-based decision making for treating respiratory diseases.

Methods: EVEREST (NCT04998604) is a phase-4, multicenter, parallel group, randomized (1:1), double-blind, active-controlled study comparing the efficacy and safety of DUP (300 mg Q2W) vs. OMZ (75–600 mg Q2W) over 24 weeks, as add-on to nasal corticosteroid therapy. Approximately 422 patients, aged ≥18 years with uncontrolled CRSwNP, ongoing symptoms of nasal congestion, loss of smell, NP score ≥5, coexisting asthma, treated with low/medium/high-dose inhaled corticosteroids and a second controller, and with an Asthma Control Questionnaire (ACQ)-5 (sum of responses to the first 5 questions derived from ACQ-7) score ≥1.5 will be recruited across 15 countries. Patients who have undergone any prior sinus surgery within 6 months and patients with conditions/concomitant diseases such as antrochoanal polyps, nasal septal deviation, acute sinusitis, nasal or upper respiratory infection, known or suspected diagnosis of cystic fibrosis and eosinophilic granulomatous with polyangiitis will be excluded. Eligibility will no longer be based on lung function and smoking history.

Results: Primary objective is to evaluate the efficacy of DUP compared to OMZ in reducing NP size and improving sense of smell (change from baseline to week 24 in NP score and University of Pennsylvania Smell Identification Test, respectively). Secondary objectives include the assessment of lung function (pre-bronchodilator forced expiratory volume in 1 second [pre-BD FEV_1]), nasal peak inspiratory flow, nasal congestion, quality of life (Sino-nasal outcome test [SNOT-22]), asthma control (visual analogue and ACQ-7), and safety.

Conclusions: EVEREST, the first head-to-head trial assessing the comparative efficacy and safety of DUP vs. OMZ in patients with severe CRSwNP and comorbid asthma will provide evidence to optimize treatment for these patients.

Funded by Sanofi and Regeneron Pharmaceuticals, Inc

S17

One-Year Results From an Open-Label Study of Donidalorsen in Patients With Hereditary Angioedema

Laura Bordone PhD, Kenneth B. Newman MD, Yiwen Deng, MS, Veronica J. Alexander PhD, Marc A. Riedl MD MS, Eugene Schneider, MD, Danny M. Cohn MD PhD

Introduction: Hereditary angioedema (HAE) is a potentially fatal disease characterised by unpredictable, recurrent, often disabling swellings. In a randomised phase 2 study (NCT04030598), participants with Type I/II HAE treated with donidalorsen reported a 90% reduction in HAE attacks, a 97% reduction starting with the second dose, and lower adverse event (AE) rates compared with placebo (71% vs 83%). We report 1-year interim analysis data from the open-label extension (OLE) study (NCT04307381) including quality-of-life (QoL), 8-week dosing, and pharmacodynamic data.

Methods: In the OLE, the on-treatment period comprised fixed (Weeks 1-13, donidalorsen 80 mg subcutaneously every 4 weeks [Q4W]) and flexible (80 mg Q4W, switched to 80 mg every 8 weeks [Q8W] or 100 mg Q4W; Weeks 17-53) dosing periods. Endpoints included treatment-emergent adverse events, monthly HAE attack rate, Angioedema Quality-of-Life Questionnaire (AE-QoL) score, and plasma prekallikrein (PKK) levels.

Results: In the OLE, participants with Type I/II HAE were enrolled (n=17). No serious AEs or discontinuation for AEs were reported. Mean reduction in HAE attacks was 94.6% (0.08/month mean monthly attack rate). During the flexible period, 8 participants switched to Q8W; 6 remained attack-free and stayed on this regimen; 2 experienced attacks and returned to Q4W. Mean HAE attack rate decreased by 75.6% in the Q8W dosing group (0.28/month mean monthly attack rate). AE-QoL total score improved by 26 points (Q8W) and 20 points (Q4W), with improvements observed in all domains. Overall plasma PKK level decreased throughout the observation period, inclusive of fixed and flexible treatment periods, through Week 53 (mean reduction 56.9%, median reduction 69.8%).

Conclusion: No safety signals were identified during the 1-year OLE. Sustained reductions in HAE attack rate and improved QoL were observed. Donidalorsen Q8W was well-tolerated and effective in reducing HAE attack rates. These results confirm prior phase 2 study findings and support continued development.

Funded by Ionis Pharmaceuticals

S18

Responsiveness to C1 Esterase Inhibitor as a Diagnostic Criterion for Hereditary Angioedema With Normal C1-INH: a Case Series

Andrew M. Smith, MD; Heidi Memmott, PharmD

Introduction: Diagnostic criteria for hereditary angioedema (HAE) with normal C1 inhibitor (C1-INH) level (HAE-nl-C1INH) includes history of recurrent angioedema; near-normal/normal levels of C4, C1-INH, and C1-INH function; and either associated genetic variant or a family history of recurrent angioedema with lack of efficacy of high-dose antihistamine therapy. Rapid and durable response to a bradykinin-targeted medication is considered supportive.

Methods: Medical records at a single center were searched retrospectively for codes for angioedema or HAE to evaluate the diagnostic process for HAE-nl-C1INH in a clinical practice setting.

Results: Three females (31-62 years; weight, 79.4-145.1 kg) with HAE-nl-C1INH were identified. All 3 patients had experienced recurrent episodes of angioedema, and antihistamine and mast cell–targeted therapies were ineffective. Laboratory testing (not during angioedema attacks) indicated near-normal/normal levels of C4, C1-INH, and C1-INH function. In 1 patient with test results during an angioedema attack, these parameters were also at near-normal/normal levels. Genetic testing was conducted for 1 patient, but no known genetic variants of HAE were detected. Diagnosis of HAE-nl-C1INH was confirmed in all 3 patients via a favorable response (symptom reduction or resolution within a few hours) after single-dose administration of intravenous rhC1-INH 50 U/kg (maximum, 4200 U) during an angioedema attack. Subsequent inclusion of rhC1-INH therapy in the HAE treatment regimen reduced angioedema attack severity in all 3 patients. Of note, 1 patient had been aware of a family history of angioedema prior to the HAE-nl-C1INH diagnosis; for the others, several family members were subsequently diagnosed with HAE-nl-C1INH.

Conclusions: Responsiveness to C1-INH replacement therapy may also be a useful supportive diagnostic criterion for HAE-nl-C1INH. A family history of recurrent angioedema may not be apparent until after the index patient is diagnosed with HAE-nl-C1INH; thus, reliance on family history diagnostic criterion may delay an accurate diagnosis and patient access to effective treatment.

Funded by Pharming

S19

Severe asthma exacerbations across disease severities: Which patients are at greatest risk?

Njira Lugogo, Ileen Gilbert, Michael Pollack, Hitesh Gandhi, Joseph Tkacz, Miguel Lanz

Rationale: The MANDALA study demonstrated a 27% reduction in severe exacerbation risk with as-needed use of albuterol-budesonide 180/160 µg fixed-dose combination versus albuterol alone in patients aged ≥12 years with moderate-to-severe asthma and ≥1 prior-year exacerbation. To understand the future exacerbation risk in the broader asthma population, we examined exacerbation occurrence across all disease severities for patients with and without a history of prior-year exacerbations.

Methods: IBM® MarketScan® databases (2010–2017) for US patients ≥12 years receiving short-acting β_2-agonists (SABA) for asthma were evaluated. Patients were indexed on a random SABA fill, had 12 months' continuous eligibility pre- and post-index, and ≥1 post-index maintenance and/or SABA claim. Severity was defined by post-index maintenance treatment step (NAEPP 2007). Post-index (12 months) severe exacerbations were compared by severity category for patients with versus without pre-index exacerbations. Data were analyzed descriptively (unadjusted chi-square and odds ratios with 95% confidence intervals; significance was set at $p \leq 0.05$).

Results: 638,931 patients ≥12 years were identified: 60.8% female; mean (standard deviation) age 34.4 (16.8) years; 52% were treated as intermittent asthma (SABA-only), 16% as mild, 9% moderate, and 23% severe persistent asthma. Overall, 43% patients had ≥1 pre-index severe exacerbation (42% of intermittent, 37% of mild, 36% of moderate, and 49% of severe persistent) and 55% had ≥1 post-index severe exacerbation (62% of intermittent, 40% of mild, 39% of moderate, and 54% of severe persistent). This represents a total of ~642,304 severe exacerbations post-index, with 40% occurring in patients with no pre-index exacerbations. For each severity level, more patients with versus without pre-index exacerbations experienced post-index exacerbations ($p<0.001$ for each). Among patients without pre-index exacerbations, depending on disease severity, 30–56% experienced ≥1 post-index exacerbation. In all patients, the odds of post-index exacerbations were greatest for patients treated as intermittent asthma versus all other severity groups ($p<0.001$ for each comparison).

Conclusion: A history of severe exacerbations is associated with a greater risk of future severe exacerbations across all disease severities in patients with asthma. Regardless of whether patients experienced exacerbations in the previous year, patients treated as intermittent asthma had greater likelihood of experiencing post-index exacerbations. Addressing symptoms and the accompanying increase in airway inflammation concomitantly with an as-needed fast-acting bronchodilator and inhaled corticosteroid, as recommended by GINA and NAEPP, may be necessary to mitigate the substantial severe exacerbation risk that exists regardless of disease severity or exacerbation history.

Funded by AstraZeneca

S20

Albuterol–budesonide Fixed-dose Combination (FDC) Inhaler As-needed Reduces Progression from Symptomatic Deterioration to Severe Exacerbation in Patients with Moderate-to-severe Asthma: Analysis from MANDALA

Bradley E. Chipps, Alberto Papi, Frank Albers, Mark Cooper, Ileen Gilbert, Carin Jorup, Frank Trudo, Christy Cappelletti, Mark Weinberg

Rationale: Short-acting β_2-agonists (SABAs) treat symptoms, but not the underlying inflammation. A "window of opportunity" may exist to prevent severe exacerbations if symptoms and inflammation are treated concomitantly, as advocated by GINA and NAEPP. In the Phase 3 MANDALA study (NCT03769090), as-needed albuterol-budesonide 180/160 µg FDC significantly reduced severe exacerbation risk by 27%, annualized severe exacerbation rate by 24%, and annualized total systemic corticosteroid exposure mean was reduced by 33% versus albuterol. This analysis of MANDALA explored the effect of as-needed albuterol-budesonide 180/160 µg on progression from symptomatic deterioration to severe exacerbation.

Methods: Symptomatic patients (N=3132) ≥4 years with moderate-to-severe asthma and ≥1 severe exacerbation in the previous year receiving ICS-containing asthma maintenance therapy were randomized 1:1:1 to as-needed albuterol-budesonide 180/160 µg, albuterol-budesonide 180/80 µg, or albuterol 180 µg. Following randomization, first symptomatic deterioration (worsening peak expiratory flow, increased study medication use or symptoms [new or worsening]) was analyzed to evaluate progression to a severe exacerbation within the subsequent 21 days.

Results: 747/1013 patients receiving albuterol-budesonide 180/160 µg and 805/1014 receiving albuterol 180 µg experienced a deterioration. Of these, 46 (6.2%) receiving albuterol-budesonide 180/160 µg and 83 (10.3%) receiving albuterol progressed to a severe exacerbation within 21 days. Albuterol-budesonide 180/160 µg reduced the risk of a progression from first deterioration to severe exacerbation by 41% versus albuterol (HR 0.59; 95%CI 0.41-0.84; p=0.004). As-needed use increased in both treatment arms around an asthma deterioration.

Conclusions: Delivering albuterol-budesonide 180/160 µg as needed during the "window of opportunity" reduced the risk of a progression from first symptomatic deterioration to severe exacerbation versus albuterol.

Funded by Bond Avillion 2 Development LP and Astra Zeneca

S21

Sustained Clinical Benefits In Patients With Chronic Rhinosinusitis With Nasal Polyps 24 Weeks Post-mepolizumab Treatment

Martin Desrosiers MD, Zuzana Diamant MD, Paolo Castelnuovo MD, Peter W Hellings MD, Joseph K Han MD, Jared Silver MD PhD, Philippe Gevaert MD, Anju T Peters MD

Introduction: SYNAPSE, a Phase 3 study in patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP), demonstrated significantly reduced disease severity with 52 weeks of 4-weekly mepolizumab 100 mg versus placebo. The durability of clinical improvements following treatment cessation has not been established.

Methods: Mepolizumab-induced effects versus placebo were evaluated for 24 weeks post-treatment. Exploratory endpoints were mean change from baseline (CFB) in: total endoscopic NP score (NPS) at Week 76 and nasal obstruction visual analogue scale (VAS) score at Weeks 73–76, in patients without surgery (analyzed post hoc); 22-item sinonasal outcome test (SNOT-22) total score at Week 76 in the overall follow-up population. Patients who withdrew from the study or had missing visit data were assigned their worst observed score prior to the missing visit.

Results: 134 patients (mepolizumab n=69; placebo n=65) entered follow-up; 26 patients with sinus surgery (mepolizumab n=6; placebo n=20) during SYNAPSE were excluded. There was a larger reduction in NPS from baseline to Week 52 with mepolizumab versus placebo (mean [SD] CFB: -1.5 [1.8] vs -0.6 [1.4]), which persisted throughout the follow-up period to Week 72 (-1.4 [1.7] vs -0.5 [1.7]). For nasal obstruction VAS score, larger improvements from baseline with mepolizumab versus placebo was maintained from Weeks 49–52 (-5.5 [2.9] vs -3.9 [3.0]) to Weeks 73–76 (-4.4 [3.2] vs -3.9 [3.3]). Larger improvements in SNOT-22 total score with mepolizumab versus placebo were maintained throughout follow-up (Week 52: -40.7 [22.4] vs -17.1 [24.7]; Week 76: -28.5 [26.8] vs -16.7 [25.8]).

Conclusions: Post-treatment, patients with severe CRSwNP maintained mepolizumab-induced improvements in NP size and symptoms. These findings suggest that targeted inhibition of interleukin-5 mediated type 2 inflammation offers a durable clinical response in these patients.

Funded by GSK [ID: 205687/NCT03085797]

S22

Clinical Remission Achievement in Severe Asthma Following Mepolizumab Treatment: Results From the REALITI-A Study at 2 Years

Guy Brusselle, MD, M. Diane Lougheed, MD, Giorgio W. Canonica, MD, Mariana Munoz-Esquerre, PhD, MD, Liam G. Heaney, MD, Robert G. Price, MSc, Peter Howarth, DM, Alejandro Raimondi, MD, Frances Gardiner, MPhil, Geoffrey Chupp, MD, Tobias Welte, MD

Introduction: On-treatment clinical remission is an ambitious clinical goal being explored in severe asthma. This real-world analysis evaluated achievement of a multi-component definition of clinical remission following mepolizumab treatment.

Methods: REALITI-A was a 2-year, observational, single-arm, prospective study, recruiting patients (≥18 years) with severe asthma newly prescribed mepolizumab (100 mg subcutaneously; physician's discretion). Data were collected for 12 months before (pre-treatment) and 24 months after mepolizumab initiation (follow-up). This post hoc analysis assessed the proportion of patients who achieved a three-component measure of clinical remission at baseline, Week 52, and Week 104. Clinical remission was defined as: 1) oral corticosteroid (OCS)-free (not receiving maintenance OCS) at assessment; 2) exacerbation-free (no exacerbations requiring OCS and/or emergency room visit/hospitalization) during pre-treatment and follow-up; and 3) Asthma Control Questionnaire (ACQ)-5 score <1.5 at assessment. Patients discontinuing mepolizumab before the time point or with missing responses in any component were considered as not achieving clinical remission.

Results: Of 822 treated patients, 214 and 184 had data available at Week 52 and 104, respectively (remaining patients excluded: missing ACQ-5 scores at Week 52/Week 104). At Week 52, 29% (n=61) of patients met the three-component definition of clinical remission versus 2% (n=4) at baseline; 39% (n=83) did not meet any of the remission criteria at baseline versus 17% (n=37) at Week 52. At Week 104, 33% (n=60) of patients met the three-component definition versus 1% (n=2) at baseline. The proportion of patients not meeting any component reduced between baseline (35%; n=64) and Week 104 (13%; n=24).

Conclusions: After 1–2 years of mepolizumab treatment, approximately one-third of patients were OCS- and exacerbation-free, with controlled symptoms, suggesting clinical remission is an achievable real-world goal for a subset of patients with severe asthma.

Funded by GSK (ID: 204710)

S23

Integrated Safety Analysis of Abrocitinib in 3802 Patients With Moderate-To-Severe Atopic Dermatitis With Over 5000 Patient-Years of Exposure

Eric L. Simpson, MD, Jonathan I. Silverberg, MD, PhD, Audrey Nosbaum, MD, Kevin Winthrop, MD, Emma Guttman-Yassky, MD, Alexander Egeberg, MD, Haiyun Fan, MS, Justine Alderfer, PharmD, Susan Johnson, MD, Saleem Farooqui, MBBS, MRCS

Introduction: Abrocitinib is efficacious and well tolerated in patients with moderate-to-severe atopic dermatitis (AD). Here, we describe the updated long-term integrated safety profile of abrocitinib in the JADE clinical program.

Methods: Analysis included 3802 patients (exposure: 5213.9 patient-years [PY]) from 7 parent phase 2/3 trials and one long-term extension trial (data cutoff September 25, 2021). Incidence rates (IRs; number of unique patients with events/100 PY) of serious adverse events (SAEs) and treatment-emergent AEs of special interest were assessed.

Results: Of the total 3802 patients in the pooled safety population, 3004 received the same abrocitinib dose throughout exposure; duration of exposure was ≥96 weeks in 26.3% of patients who received abrocitinib 200 mg (n=1981) and 41.3% of patients who received abrocitinib 100 mg (n=1023). Median age was 30.0 years. Incidence was higher in older (≥65 years, n=146) versus younger (18 to <65 years, n=2368) patients for SAEs (17.6 [95% CI: 11.7-25.5] vs 6.7 [5.8-7.8]), herpes zoster (HZ, 8.1 [4.3-13.8] vs 3.8 [3.1-4.6]), malignancy (excluding nonmelanoma skin cancer, 2.4 [0.6-6.0] vs 0.1 [0.0-0.4]), major adverse cardiac events (1.2 [0.1-4.2] vs 0.3 [0.1-0.6]), thrombocytopenia (confirmed platelet count $<75\times10^3/mm^3$, 1.8 [0.4-5.1] vs 0.3 [0.1-0.6]), and lymphopenia (3.5 [1.3-7.6] vs 0.1 [0.0-0.3]). The most frequent serious infections with abrocitinib 200 mg and 100 mg were HZ (0.5% and 0.2%), herpes simplex (0.1% with either dose), and pneumonia (0.2% with either dose).

Conclusions: Abrocitinib has an acceptable long-term safety profile with >5000 PY of exposure in appropriate patients with moderate-to-severe AD.

Funded by Pfizer, Inc

S24

The Impact of Abrocitinib on Vaccine-Induced Immune Responses in Adolescents With Moderate-to-Severe Atopic Dermatitis Undergoing Routine Tetanus, Diphtheria, and Pertussis Vaccination in Phase 3 JADE TEEN

Michael Cork, MD, Lawrence Eichenfield, MD, Carsten Flohr, PhD, Christine Bangert, MD, Sebastien Barbarot, MD, Gary Chan, PhD, Ricardo Rojo, PhD, Fan Zhang, PhD, Claire Feeney, MD, Hernan Valdez, MD

Introduction: It is currently unclear whether abrocitinib, a Janus Kinase-1 inhibitor, has an impact on the immunogenicity of routine vaccinations in adolescents with moderate-to-severe atopic dermatitis. We assessed the effect of abrocitinib on mounting immune responses to the tetanus, diphtheria, and acellular pertussis (Tdap) booster vaccination in adolescent patients from the JADE TEEN trial (NCT03796676).

Methods: Adolescents (aged 12-17 years) received abrocitinib (200 mg/100 mg) or placebo orally, once-daily for 12 weeks with medicated topical therapy; a subset (n=25) received the Tdap vaccine at week 8. The proportion of patients who achieved a ≥4-fold increase in IgG concentrations to vaccine antigens from baseline (week 8) to 4 weeks post-vaccination (week 12), routinely considered a satisfactory response, was assessed.

Results: Patients receiving abrocitinib 200 mg (n=6), abrocitinib 100 mg (n=9), or placebo (n=10) were administered Tdap vaccination per local guidelines. At 4 weeks post-vaccination, serum samples were available for 4 (abrocitinib 200 mg), 8 (abrocitinib 100 mg), and 10 (placebo) patients. A ≥4-fold increase in antibody concentration to tetanus toxoid was achieved in 100%, 75%, and 50% of patients in the abrocitinib 200 mg, 100 mg, and placebo groups, respectively; in 100%, 62.5%, and 80% to diphtheria toxoid; in 100%, 75%, and 70% to pertussis toxin; in 100%, 62.5%, and 70% to filamentous hemagglutinin; in 0%, 0%, and 10% to fimbriae types 2/3; and in 100%, 87.5%, and 80% to pertactin. Treatment-emergent adverse events occurred in 16.7% (1/6, abrocitinib 200 mg), 33.3% (3/9, abrocitinib 100 mg), and 10.0% (1/10, placebo) of patients; none were severe, serious, or led to discontinuation.

Conclusions: There were no appreciable differences in immune responses to Tdap vaccination in adolescents receiving abrocitinib compared to placebo. Despite the limited sample size of the current study, the results suggest adequate immune responses to the Tdap vaccine.

Funded by Pfizer Inc.

S25

HAE abdominal episode with concurrent acute appendicitis in a 7 yo M

Ali Doroudchi, Carine Tamamian, Sophia Quiroz, Chantal Elizaga, and Raffi Tachdjian

Rationale: Hereditary angioedema (HAE) is a bradykinin-mediated disorder in which patients experience unpredictable episodic angioedema involving skin and mucosal tissue. We present a young boy with type 1 HAE presenting with acute abdominal pain found to have concurrent acute appendicitis during an abdominal HAE episode.

Methods: C1 esterase inhibitor level and function, C4, Invitae HAE Gene Panel

Results: A newly diagnosed 7-year-old male presented with sudden onset lower abdominal pain accompanied by nausea and emesis. On exam, patient was tired-appearing, pale, diaphoretic, with a tender abdomen and absent bowel sounds. Given concern for a surgical abdomen, he was referred to the ER, where WBC was 17.7 x10E3/uL with 83% neutrophils, and non-compressible appendix was seen on ultrasound, with visualized appendicolith and peri-appendiceal free fluid indicative of acute appendicitis. C4 was undetectable (<2 mg/dL). Given a high suspicion for acute abdomen in the setting of HAE swelling, 20 units/kg Berinert were administered along with antibiotics parenterally. The following morning, surgical over medical management was agreed upon with the family. Laparoscopic appendectomy was uncomplicated and suggestive of acute appendicitis intra-operatively and later confirmed on pathology examination. C1 esterase inhibitor level and function ultimately returned as undetectable (<8 mg/dL) and 16%, respectively. Upon further discussion with the patient's family during follow up, it was decided to obtain genetic testing, with a suspicion that he may have a *de novo* variant causing his phenotype. A hereditary angioedema gene panel (Invitae) confirmed a pathogenic variant in *SERPING1* (exon 1-4 deletion), not present in either parent on further testing.

Conclusions: We present a challenging case in which a young boy with HAE presented with concurrent acute appendicitis. This case highlights the importance of keeping a high index of suspicion for "common" etiologies of abdominal pain, even in patients with less common and established diagnoses such as HAE.

S26

Berotralstat Improved Quality of Life through 96 Weeks Across Multiple Subgroups of Patients with Hereditary Angioedema

Daniel F. Soteres, William R. Lumry, Markus Magerl, Remi Gagnon, Bhavisha Desai, Dianne Tomita, Douglas T. Johnston, Marcus Maurer on behalf of the APeX-2 Investigators

Introduction: Berotralstat is a first-line, once-daily (QD) oral prophylaxis for hereditary angioedema (HAE) shown to reduce the burden of disease and treatment.[1,2] We present patient-reported quality of life (QoL) in patients who received berotralstat in APeX-2 (NCT03485911).

Methods: QoL was assessed using the validated Angioedema-QoL questionnaire (AE-QoL), and stratified by baseline age, sex, attack rate, prior prophylaxis, and by incidence of gastrointestinal adverse events (GI AEs) during berotralstat therapy. Decreasing scores indicated QoL improvement. The minimal clinically important difference (MCID) is a 6-point reduction in the total AE-QOL score.

Results: In patients who received berotralstat 150 mg (N=40) mean (SEM) improvements from baseline to Week 96 in total AE-QoL score exceeded the MCID value from Week 4 and were sustained through 96 weeks when stratified by age (Week 96, <35 years, -23.6 [7.9]; 35–50 years, -21.4 [2.5]; >50 years, -24.5 [6.9]), sex (female, -23.9 [4.6]; male, -21.7 [6.0]), baseline attack rate (<2/month, -24.7 [8.9]; ≥2/month:,-22.4 [3.9]), and prior prophylaxis (prior androgens, -19.4 [5.3]; prior C1 inhibitor, -21.6 [3.8]). Mean (SEM) total AE-QoL score improved from baseline to Week 96 regardless of the presence (n=11; -18.2 [4.9]) or absence (n=8; -29.5 [4.4]) of GI AEs during the first 24 weeks on berotralstat. Improvements were reflected across all QoL domains (functioning, fatigue/mood, fear/shame, nutrition) through 96 weeks irrespective of stratification. Across most subgroups, the largest improvement occurred in the functioning domain.

Conclusions: Long-term prophylaxis with berotralstat led to sustained and clinically meaningful improvements in patient-reported QoL across multiple subgroups, suggesting sustained reductions in disease and treatment burden.

Funded by BioCryst

S27

Consistently Low Hereditary Angioedema Attack Rates Observed with Berotralstat Regardless of Previous Prophylaxis: Real-World Outcomes

Marc A. Riedl, Bhavisha Desai, Alex Tilley, Douglas T. Johnston, Stephanie Wasilewski, Jonathan A. Bernstein

Introduction: Clinical trial data showed patients who switched to oral berotralstat monotherapy reported consistently low hereditary angioedema (HAE) attack rates. Here we present preliminary effectiveness data of patients in the United States who initiated berotralstat treatment in the real-world clinical setting and were previously on another prophylactic therapy.

Methods: Data was collected through the sole-source pharmacy and included patients with confirmed HAE Type I/II who actively received berotralstat 110 or 150mg from 12/16/2020-5/20/22 and were stratified by previous prophylaxis. Baseline attack rates were reported for the 90 days prior to berotralstat initiation. While on therapy, median attacks/month (25^{th},75^{th} percentile) were calculated over each 90-day period by averaging each patient's monthly reported attack rate (1 month=~28 days). Some patients did not report attack rates at each refill.

Results: In patients treated with prior prophylaxis (n=129) the median baseline attack rate was 1.7 attacks/month which decreased to 0.3 (0,1.31) from days 1-90; 0.6 (0,1.00) from days 91-180; 0.5 (0.25,1.00) from days 181-270; and 0.5 (0,1.50) from days 271-360. Specifically, in the lanadelumab group (n=53), the baseline attack rate of 1.0 attack/month decreased to 0 (0,0.50) from days 1-90; 0.3 (0,0.75) from 91-180; 0.5 (0,1.00) from 181-270; and 0.5 (0,1.38) from 271-360. In the subcutaneous C1-inhibitor group (n=31), the baseline attack rate of 1.7 attacks/month decreased to 0.8 (0,2.00) from days 1-90; 0.7 (0,2.08) from 91-180; 1.0 (0.54,1.50) from 181-270; and 1.0 (0.29,2.17) from 271-360. Patients without prior prophylaxis (n=112) had similar attack rate reductions. The most common adverse events reported were consistent with clinical trials.

Conclusions: Patients previously treated with another prophylactic therapy reported consistently low HAE attack rates when treated with once daily berotralstat.

Funded by BioCryst

S28

Successful Use of Dupilumab for Solar Urticaria

Katie Smiley PA-C, Lauren Loop, Bob Geng MD

Introduction: Solar urticaria represents a rare form of physical urticaria distinct from photodermatitis. Symptoms can be disruptive and disabling, limiting patients to indoor activities and restricted quality of life. There are no formal guidelines for management of solar urticaria, but recommendations include limiting sun exposure, broad spectrum sunscreens and oral second generation antihistamines.

Case presentation: We present the case of a 50 year old male with a two year history of intermittent erythematous, edematous, pruritic and painful urticaria in sun exposed areas. Lesions last 1-3 hours, without systemic symptoms. Clinical diagnosis was confirmed in clinic with development of diffuse pruritic erythema to sun exposed areas after 10 minutes in natural sunlight. He failed several 4x maximum dose antihistamines (cetirizine, hydroxyzine, levocetirizine) though could only tolerate limited use due to drowsiness, as well as adjunctive medications (ranitidine, famotidine and montelukast). He started omalizumab 300 mg monthly; then increased to 300 mg twice monthly; both without improvement. Omalizumab was discontinued due to lack of improvement compared to use of very high dose cetirizine alone, typically 60-80 mg, sometimes up to 100 mg daily as needed. Onset of urticaria became faster after sun exposure. He started dupilumab 300 mg every 2 weeks with a 600 mg loading dose with significant improvement of symptoms after his second injection with concurrent use of cetirizine 20 mg daily to twice daily, without drowsiness. Since clinical improvement, the patient notes only two breakthrough episodes of urticaria, the most recent reaction occuring off cetirizine. He has a significant increase in quality of life and is now able to go out on short outdoor walks without physical coverings/sunscreen.

Discussion: This patient's case demonstrated the successful use of dupilumab, in combination with tolerated dose of oral antihistamines, with improvement of refractory solar urticaria.

S29

Use of Over-the-Counter Products to Treat Severe Allergic Reactions Before an Epinephrine Auto Injection Device: Results of a Patient/Caregiver Survey

Richard Lowenthal, Erin Rooney, Sarina Tanimoto, Harris Kaplan,, Ayman Kafal

Rationale: Immediate intramuscular administration of epinephrine is first-line treatment for severe allergic reactions. Although progression of an allergic reaction can be quick and unpredictable, patients/caregivers often "wait and see," administering over-the-counter (OTC) products (typically antihistamines) before epinephrine. Understanding factors contributing to epinephrine delay and reducing these delays is key to improving outcomes.

Methods: To gather insights regarding OTC product use after initial allergy symptoms, a 20-minute double-blind survey was conducted with patients/caregivers who used an epinephrine injectable device within the preceding 12 months. Respondents answered questions about their/their child's allergy, current treatment, and the number of minutes they delayed using the device.

Results: Two-hundred individuals responded. Average time between symptom development and device use was 8.8 minutes; fear of the needle was the main reason for delay. Of the 200 respondents, 91% reported using an OTC product alone or prior to using their injectable epinephrine device some of the time. 51% of respondents used an OTC medication approximately 50% of the time. 63% of respondents used an OTC product before their epinephrine injectable device ≥50% of the time. Respondents indicated they would use a needle-free delivery device for administering epinephrine as an initial treatment rather than an OTC product 72% of the time.

Conclusions: Despite the unpredictable progression of allergic reactions to serious/fatal outcomes, and the ineffectiveness of OTC products, 91% of respondents reported using an OTC product as sole or initial treatment. The majority of respondents reported they would use a needle-free option for administering epinephrine instead of or before an OTC product.

Funded by ARS Pharmaceuticals, Inc.

S30

Epinephrine Intranasal Spray 2.0 mg Versus Epinephrine Injection Products: An Integrated Pharmacokinetic Analysis

Jay A. Lieberman, Jay Portnoy, Michael Kaliner, Richard Lockey, Thomas B. Casale, Richard Lowenthal, Sarina Tanimoto, Ayman Kafal

Rationale: ARS-1, an intranasal (IN) epinephrine spray, is under development as a needle-free alternative to manual intramuscular (IM) epinephrine injection and epinephrine injection devices for severe allergic reactions. We therefore performed an integrated analysis of 5 clinical studies to evaluate ARS-1's pharmacokinetic (PK) and pharmacodynamic (PD) effects versus IM epinephrine.

Methods: Healthy volunteers and subjects with allergic rhinitis received ARS-1 (2.0 mg), epinephrine auto-injector (0.3 mg), or IM epinephrine injection (0.3 mg) and differences in PK and PD parameters were assessed.

Results: 78 subjects received ARS-1 2.0 mg, 77 received epinephrine via an auto-injection device 0.3 mg, and 178 received manual IM injection 0.3 mg via healthcare provider. Following a single dose, mean C_{max} values (pg/mL) were 485, 581, and 277 for ARS-1, auto-injector, and IM injection, respectively. Median t_{max} (minutes) was shortest for auto-injector (10), followed by ARS-1 (20.5), and IM injection (45). Single-dose systolic blood pressure, diastolic blood pressure, and heart rate E_{max} values were comparable for ARS-1, (22.3, 8.99, and 17.8) and auto-injector (18.2, 6.48, and 14.8), respectively; PD responses were lower for IM injection (11.6, 5.44, and 11.5). Similar trends were observed following 2 doses.

Conclusion: Consistent with previous reports, this integrated analysis demonstrates differences in PK and PD parameters between IM injection products despite them being considered clinically indistinguishable. The PK and PD profiles of ARS-1 2.0 mg fell within the range of those of approved IM- and auto-injection treatments of allergic reactions including anaphylaxis. Thus, ARS-1 may represent a reliable, needle-free option to epinephrine injection products.

Funded by ARS Pharmaceuticals, Inc

S31

The Predictors of Eosinophilia in Patients with Severe Asthma

Racha Abi Melhem, M.D, Marc Assaad, M.D, Khalil El Gharib, M.D, Samer Asmar, M.D, Ahmad Itani, M.D

Introduction: Asthma is classified into 2 subtypes; Eosinophilic asthma (EA) and Non-eosinophilic asthma (NEA), based on the underlying immune mechanism. The aim of our study is to identify markers associated with the development of eosinophilia in the setting of severe asthma.

Methods: The National Inpatient Sample Database was used to sample individuals into 2 groups: eosinophilic and non-eosinophilic severe asthma. Demographics and comorbidities were collected using ICD-10 codes. Patients with restrictive, other types of obstructive lung diseases, conditions associated with eosinophilia, allergic bronchopulmonary aspergillosis and patients declared dead on arrival were excluded. Propensity score matching using a 1:2 matching ratio was performed to match individuals by demographics and comorbidities. A logistic regression model was used to generate a propensity score. A p-value of <0.05 was considered statistically significant.

Results: Out of 2,646 patients included in the study, 882 patients had severe asthma with eosinophilia.
Severe EA group was characterized by increased steroid use (18.3% vs 9.5%; $p<0.001$), status asthmaticus (10.4% vs 7.4%; $p<0.009$), family history of asthma (4.4% vs 2.4%; $p<0.004$), allergies (20.7% vs 17.2%; $p= 0.028$), allergic rhinitis (4% vs 1.2%; $p<0.001$), nasal polyps (1.9% vs 0.1%; $p<0.001$) and allergic dermatitis (3.7% vs 0.4%; $p<0.001$) compared to NEA group. The need for mechanical ventilation and supplemental oxygen was also higher among EA group ($p< 0.001$ for both), however there were no significant difference in mortality rate and the length of hospital stay was similar in both groups.

Conclusion: Prompt detection of predictors of eosinophilia, in patients with non-severe asthma, might benefit from earlier management with immune targeted therapy, used to reduce progression of asthma into its severe form. Larger scale studies are needed to better explore this association.

S32

Uncovering the Hidden Danger: When Contact Dermatitis Conceals Hypereosinophilic Syndrome

Charu Debnath MD, Laura Chong MD, Dean Atkinson MD

Introduction: Hypereosinophilic syndrome (HES) is a group of rare disorders characterized by absolute eosinophil count $\geq 1.5 \times 10^9$/L and associated with multiorgan damage. With clinical manifestations ranging from pruritus to life threatening cardiovascular disease, increased awareness and early diagnosis can lead to better outcomes.

Methods: We present a case of HES initially diagnosed and treated as contact dermatitis.

Results: A 21-year-old female was referred to our clinic by her dermatologist for workup of severe dermatitis along with request for patch testing. The patient reported an 8-month history of rash on her face and chest. She denied hives, cough, chest pain, rhinosinusitis, gastric symptoms, new foods or medications. Although initially diagnosed with contact dermatitis from her sunscreen, the rash persisted despite avoidance. Patch testing was positive for amerchol and formaldehyde. A complete blood count showed persistent hypereosinophilia (initial 11843/mcL). Workup for eosinophilia revealed an increased tryptase level (19.8 mcg/L) but negative for secondary causes, leading to a diagnosis of idiopathic HES. While initially on high dose prednisone and hydroxyurea with poor response, switching to mepolizumab resulted in complete resolution of the rash and normalization of eosinophil count.

Conclusion: Hypereosinophilic syndrome is a rare condition, with an incidence of 0.315 to 6.3 per 100,000 people in the US. Mean age at diagnosis is 43-48 years old with more men affected. Skin, pulmonary, and gastrointestinal symptoms are common, and cardiac involvement can be fatal. As HES is a diagnosis of exclusion, a thorough workup for infectious, autoimmune, neoplastic, and allergic/atopic causes is essential. Our patient's case was unique as she was a young female with only skin involvement. With earlier studies reporting a mean survival of 9 months, early diagnosis and prompt treatment with targeted therapies can greatly improve patient outcomes.

S33

Efficacy and Safety of Subcutaneous Garadacimab for the Prophylaxis of Hereditary Angioedema Attacks in Adults and Adolescent Patients with HAE: Results from a Multicenter, Placebo-Controlled Phase 3 Trial

Timothy J Craig, Markus Magerl, Avner Reshef, H Henry Li, Joshua S Jacobs, Jonathan A Bernstein, Henriette Farkas, William H Yang, Erik S G Stroe[0], Isao Ohsawa, Raffi Tachdjian, Michael E Manning[13], William R Lumry, Inmaculada Martinez Saguer, Emel Aygören-Pürsün, Bruce Ritchie, Gordon L Sussman, John Anderson, Kimito Kawahata, Yusuke Suzuki, Petra Staubach, Regina Treudler, Henrike Feuersenger, Lolis Wieman, and Iris Jacobs.

Background: The efficacy and safety of garadacimab, a fully human immunoglobulin G4 monoclonal antibody targeting activated factor XII for the prevention of hereditary angioedema (HAE) attacks, were evaluated in a randomized, placebo-controlled, 6-month, Phase 3 trial (NCT04656418).

Methods: Patients aged ≥12 years with type I/II HAE were randomized (3:2) to receive monthly subcutaneous (SC) garadacimab 200 mg or placebo, after an initial SC loading dose of garadacimab 400 mg or volume-matched placebo. Efficacy, safety, and quality-of-life (QOL) measures were assessed.

Results: Once-monthly SC garadacimab significantly reduced the attack rate (AR) compared with placebo ($p<0.001$), resulting in an AR reduction of 86.5% (95% CI: 57.8–95.7). Adjusted for baseline AR, garadacimab-treated patients (n=39) experienced mean monthly ARs of 0.22 vs 2.07 for placebo-administered patients (n=24), resulting in an AR reduction vs placebo of 89.2% (95% CI: 75.6–95.2). Twenty-four (61.5%) garadacimab-treated patients were attack-free during the 6-month study, and 74.4% achieved ≥90% attack reduction vs the run-in period. The time to first attack was ≥72 days for 75% of garadacimab-treated patients vs 5 days for placebo-administered patients. Forty (62.5%) patients experienced ≥1 treatment-emergent adverse event (TEAE), totaling 129 events, including one serious, severe TEAE in the garadacimab arm (laryngeal attack managed with overnight hospitalization and assessed as not related to garadacimab by the investigator). Mild injection-site reactions occurred in 2 garadacimab (5%) and 3 placebo (12%) patients. No adverse events led to discontinuation. Angioedema-QOL total mean score improved by 23.7 points following the first garadacimab administration.

Conclusions: Once-monthly SC garadacimab was well tolerated throughout the treatment period and significantly reduced the AR vs placebo in patients with HAE.

Funded by CSL Behring

S34

Garadacimab for hereditary angioedema prophylaxis in adolescents: efficacy and safety from the VANGUARD Phase 3 and 3b open-label extension trial (first interim analysis)

Markus Magerl, Inmaculada Martinez-Saguer, Joshua S Jacobs, H Henry Li, Jonathan A Bernstein, Connie Hsu, Karl V Sitz, Ingo Pragst, Henrike Feuersenger, Lolis Wieman, Maressa Pollen, Avner Reshef

Background: Efficacy and safety of garadacimab (fully human monoclonal antibody targeting activated factor XII) for prophylaxis of hereditary angioedema (HAE) attacks were demonstrated in the Phase 2 (adults only) [1] and pivotal Phase 3 (VANGUARD) studies [2]. Here, adolescent safety and efficacy data from the pivotal Phase 3 study and open-label extension (OLE, first planned analysis; NCT04739059) are reported.

Methods: In the Phase 3 study, after ≥1-month run-in, six adolescents (12–≤17 years old, HAE type I/II) were randomized to receive once-monthly subcutaneous garadacimab 200 mg (n=4) or placebo (n=2) for 6 months after garadacimab 400 mg loading dose or volume-matched placebo. All entered the OLE plus five garadacimab-naïve adolescents (n=10, one aged 18 in OLE excluded). Time-normalized monthly attack rate during the treatment period was compared against run-in.

Results: At OLE first planned analysis, garadacimab exposure ranged from 3.3–15.2 months. No serious treatment-emergent adverse events (TEAEs), TEAEs leading to discontinuation, special interest TEAEs, treatment-related TEAEs, or injection-site reactions were reported. In the Phase 3 study, 4/6 adolescents (66.7%; 2 treated, 2 placebo) experienced ≥1 TEAE (11 reported; all mild or moderate) and in the OLE, 6/10 adolescents (60.0%) experienced ≥1 TEAE (20 reported; all mild or moderate). In the phase 3 study, 2/4 garadacimab-treated adolescents (50.0%) were attack-free during treatment and maintained attack-free status in OLE. One garadacimab-treated adolescent who initially experienced a 5.8% increase in attack rate vs run-in, achieved a 45.5% reduction in OLE. In the OLE, 3/5 adolescents were attack-free; one achieved 93.8% reduction over 15.2 months, and one achieved 65.7% reduction over 3.3 months vs run-in.

Conclusions: Consistent with adult data, once monthly garadacimab demonstrated a favorable safety profile and had sustained efficacy as routine prophylaxis to prevent HAE attacks in adolescents.

Funded by CSL Behring