Eastern Allergy Conference
May 30 - June 2, 2024 ~ Palm Beach, FL

Scientific Posters F1-F41 will be on display in the Ponce Foyer during the coffee break, 10:00-10:45am, Friday May 31, 2024

Not for CME Credit

F1

Impact Of Food Allergy On Work Productivity And Healthcare Resource Use In Patients With Allergic Asthma Treated With Omalizumab

Panida Sriaroon, MD; Ignacio J. Ansotegui, MD, PhD; Alessandro Fiocchi, MD; R. Sharon Chinthrajah, MD; Sachin Gupta, MD, S. Shahzad Mustafa, MD; My Hanh Zacharia, PharmD; Briana Cameron, PhD; Pranil Raut, MS; David M. Fleischer, MD

Introduction: Omalizumab is effective for the treatment of moderate-to-severe allergic asthma. However, the impact of comorbid food allergies (FA) on work productivity/activity impairment and healthcare resource use (HRU) in patients treated with omalizumab is unclear.

Methods: In this post-hoc analysis of EXCELS, a prospective, observational study (NCT00252135), patients aged ≥12 years with moderate-to-severe allergic asthma were grouped by FA diagnosis, and categorized as omalizumab new starters (n=587; started omalizumab ≤7 days before to 30 days after baseline visit), omalizumab established users (n=4419; started omalizumab >7 days before baseline visit), or non-omalizumab users (n=2830). The impact of baseline FA on Work Productivity and Activity Impairment (WPAI-Asthma) overall scores, and HRU (steroid bursts and emergency department visits) was determined for up to 5 years.

Results: Regardless of the presence or absence of FA, both new starters and established users of omalizumab had improvements in mean WPAI overall scores by 12 months (FA/non-FA; new starters: baseline, 35.9/33.6; month 12, 21.7/18.9; established users: baseline, 23.1/23.1; month 12, 20.7/20.7). For HRU, regardless of the presence or absence of FA, both new starters and established users of omalizumab had similar improvements over time in mean steroid bursts (FA/non-FA; new starters: baseline, 2.8/2.8; month 12, 0.8/0.5; established users: baseline, 2.3/2.2; month 12, 0.8/0.7), and mean emergency department visits (FA/non-FA; new starters: baseline, 1.2/1.1; month 12, 0.2/0.2; established users: baseline, 1.0/0.8; month 12, 0.1/0.2).

Conclusions: In patients with asthma treated with omalizumab, work productivity/activity impairment and HRU were improved over time, regardless of the presence or absence of comorbid FA.

Funding: Analysis was funded by Genentech, Inc., a member of the Roche Group.

F3

Tapinarof Cream 1% Once Daily: Significant Efficacy in the Treatment of Atopic Dermatitis in Two Pivotal Phase 3 Trials in Adults and Children Down to 2 Years of Age

Jonathan I. Silverberg, Lawrence F. Eichenfield, Adelaide A. Hebert, Eric Simpson, Linda Stein Gold, Robert Bissonnette, Kim A. Papp, John Browning, Pearl Kwong, Neil J. Korman, Philip M. Brown, David S. Rubenstein, Stephen C. Piscitelli, Matthew C. Somerville, Anna M. Tallman, Leon Kircik

Introduction: Tapinarof is a non-steroidal, topical aryl hydrocarbon receptor agonist approved for the treatment of plaque psoriasis in adults, and under investigation for plaque psoriasis in children down to 2 years of age and for the treatment of atopic dermatitis (AD) in adults and children. ADORING 1 and 2 were two identical, pivotal, phase 3, randomized, double-blind, vehicle-controlled trials of tapinarof cream 1% once daily (QD) in adults and children down to 2 years of age with AD. Here, we present phase 3 efficacy and safety results.

Methods: Patients with Validated Investigator Global Assessment for Atopic Dermatitis™ (vIGA-AD™) score ≥3, Eczema Area and Severity Index (EASI) ≥6, and body surface area (BSA) involvement of 5-35% received tapinarof or vehicle QD for 8 weeks. Primary endpoint was vIGA-AD™ response (score of clear [0] or almost clear [1] and ≥2-grade improvement). Secondary endpoints included ≥75% improvement in EASI score (EASI75), and ≥4-point reduction in Peak Pruritus-Numerical Rating Scale (PP-NRS; aged ≥12 years). Incidence of adverse events (AEs) was recorded.

Results: 407 and 406 patients were randomized in ADORING 1 and 2. At baseline, 84.0-89.9% of patients had vIGA-AD™=3, mean EASI=12.5-13.3, and mean BSA affected=16.7-16.9%. At Week 8, primary and secondary endpoints were met with statistical significance in tapinarof groups versus vehicle: vIGA-AD™ response, 45.4% vs 13.9% and 46.4% vs 18.0% (both $P<0.0001$); EASI75 response, 55.8% vs 22.9% and 59.1% vs 21.2% (both $P<0.0001$); and ≥4-point reduction in PP-NRS, 55.8% vs 34.2% ($P=0.0366$) and 52.8% vs 24.1% ($P=0.0015$), in ADORING 1 and 2, respectively. Most AEs were mild or moderate, with low trial discontinuation rates due to AEs. Most common AEs were folliculitis, headache, and nasopharyngitis.

Conclusion: Tapinarof cream was efficacious and well-tolerated in adults and children down to 2 years of age with AD.

Funding: Dermavant Sciences, Inc.

F4

The impact of mepolizumab on fatigue and work impairment in patients with chronic rhinosinusitis with nasal polyps (CRSwNP): Analysis from SYNAPSE study

Jared Silver MD PhD, Peter Howarth MBBS DM FRCP, Robert Chan MD, Lingjiao Zhang PhD, Steven Smith PhD, Joaquim Mullol MD PhD, Claus Bachert MD PhD, Wytske Fokkens MD PhD

Introduction: Chronic rhinosinusitis with nasal polyps (CRSwNP) may cause sleep disturbances and fatigue. This post hoc analysis of SYNAPSE explored the effect of mepolizumab and impact of comorbidities and blood eosinophil count (BEC) on fatigue and work impairment in patients with CRSwNP.

Methods: SYNAPSE was a double-blind, placebo-controlled, multicenter Phase III study in patients with severe CRSwNP. Eligible patients randomized 1:1 received mepolizumab 100mg or placebo subcutaneously every 4 weeks for 52 weeks plus standard of care. The impact of mepolizumab treatment, comorbidities and BEC on change from baseline in the fatigue domain of the SinoNasal Outcomes Test-22 Item (SNOT-22; range: 0-20) and Work Productivity and Activity Impairment (WPAI; range 0–100%) scores at Week 52 were assessed.

Results: Overall, 289/407 patients (71%) had comorbid asthma, 108/407 (27%) had comorbid non-steroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD), while 278/407 (68%) had BEC ≥300 cells/µL. Change from baseline to Week 52 in SNOT-22 fatigue domain score was higher in patients treated with mepolizumab versus placebo (treatment difference [95% confidence interval {CI}]: -3.4 [-4.7,-2.0]; p<0.001). Numerical improvements were observed irrespective of comorbid asthma (treatment difference [95% CI] in patients with asthma: -3.1 [-4.8,-1.4; p<0.001]; patients without: -3.3 [-6.2,-0.5; p=0.021]) or N-ERD (treatment difference [95% CI] in patients with N-ERD: -3.6 [6.2,-1.0; p=0.008]; patients without: -2.9 [-4.6,-1.2; p=0.001]), but not BEC (treatment difference [95% CI] in patients with BEC <300 cells/µL: -2.1 [-4.8,0.6; p=0.122]; patients with BEC ≥300 cells/µL: -3.8 [-5.5,-2.1; p<0.001]). In addition, patients treated with mepolizumab versus placebo had numerically lower WPAI score for overall work impairment (treatment difference [95% CI]: -5.8 [-12.3,0.6; p=0.078]).

Conclusions: Patients with CRSwNP treated with mepolizumab versus placebo had greater improvements in fatigue, irrespective of respiratory comorbidities and in the setting of BEC elevation; work impairment was also numerically reduced with mepolizumab.

Funding: GSK [GSK ID: 205687/NCT03085797].

F5

Clinical remission (CR) in patients with severe eosinophilic asthma (SEA): an analysis of SIROCCO and CALIMA trial data

Andrew Menzies-Gow, PhD; Flavia L. Hoyte, MD; David B. Price, FRCGP; Sean Swisher, PharmD; David Cohen, PhD; Anat Shavit, DVM

Introduction: Studies have shown CR is achievable in patients with SEA receiving benralizumab. This post-hoc analysis evaluated baseline characteristics of patients in the Phase 3 SIROCCO (NCT01928771) and CALIMA (NCT01914757) trials who achieved CR or did not (non-CR).

Methods: Eligible patients were aged 12–75 years with ≥2 exacerbations within the previous year despite medium- to high-dose inhaled corticosteroids plus additional controllers. Patients on oral corticosteroids (OCS) at baseline were excluded. CR was defined as meeting the following three components: zero exacerbations, zero OCS, and a 6-Item Asthma Control Questionnaire (ACQ-6) score of <1.5 after 12 months.

Results: Of 1123 patients, 39.2% (213/544) receiving benralizumab achieved CR versus 26.6% (154/579) receiving placebo. Baseline median [range] blood eosinophil counts were higher among patients achieving CR (benralizumab, 412 [0, 2095]; placebo, 402 [10, 3640] cells/µL) than non-CR patients (benralizumab, 365 [0, 3100]; placebo, 360 [0, 2610] cells/µL). More CR patients had a forced expiratory volume in 1 second of ≥65% predicted (benralizumab, 38.7%; placebo, 40.9%) than non-CR patients (benralizumab, 29.4%; placebo, 33.8%). In the benralizumab group, a higher percentage of CR patients (19.7%) had history of nasal polyps, than non-CR patients (11.5%). The proportion of patients with >2 exacerbations within 12 months of baseline was lower among CR patients (benralizumab, 28.6%; placebo, 26.0%) than non-CR patients (benralizumab, 34.7%; placebo, 38.8%). Mean [standard deviation] baseline ACQ-6 scores were lower among CR patients (benralizumab, 2.5 [0.86]; placebo, 2.5 [0.87]) than non-CR patients (benralizumab, 3.0 [0.85]; placebo, 2.9 [0.88]).

Conclusions: CR patients had higher blood eosinophils, better lung function, fewer exacerbations, and lower ACQ-6 scores at baseline than non-CR patients. In the benralizumab group, more CR patients had history of nasal polyps than non-CR patients. These data highlight the importance of diagnosing and appropriately treating SEA as early as possible.

Funding: AstraZeneca

F6

ROCATINLIMAB DEMONSTRATES IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES IN ADULT PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS IN A PHASE 2B TRIAL

Eric Simpson, MD; Angela Williams, PhD; Camilla Chong, MD; Ehsanollah Esfandiari, MD, PhD

Introduction: Patients with moderate-to-severe atopic dermatitis (msAD) often experience chronic cycles of pruritus and scratching, affecting sleep and quality-of-life. Rocatinlimab, an anti-OX40 monoclonal antibody, is being evaluated for the treatment of msAD (Guttman-Yassky E, et al. Lancet. 2023;401:204-14). We present patient-reported outcomes (PROs) in adult patients with msAD receiving rocatinlimab.

Methods: This Phase 2b, double-blind, placebo-controlled trial (NCT03703102) randomized patients (n=274) 1:1:1:1:1 to subcutaneous rocatinlimab 150 or 600mg every 4 weeks for 36 weeks, 300 or 600mg every 2 weeks for 36 weeks, or placebo (Weeks 0–18; rocatinlimab 600mg every 2 weeks from Week 18 to Week 36), and a 20-week off-treatment follow-up (Week 56). PROs included pruritus and sleep disturbance (SD) scores, measured using a Numerical Rating Scale (NRS), and the Dermatology Life Quality Index (DLQI), assessed at baseline at every study visit until Week 56.

Results: Overall, 267 patients received rocatinlimab (n=210) or placebo (n=57). From baseline to Week 16, percentage reductions in NRS-pruritus (rocatinlimab, –25.6% to –48.0%; placebo, –6.2%; $p \leq 0.029$) and NRS-SD scores (rocatinlimab, –41.6% to –7.0%; placebo, +46.5%; $p \leq 0.025$) were greater with rocatinlimab vs placebo. Improved pruritus and SD scores with rocatinlimab were maintained until Week 56. Greater reductions in DLQI scores, indicating improved health-related quality-of-life, were observed with rocatinlimab (–2.6 to –6.3) vs placebo (+0.2) at Week 16 (all $p<0.05$). DLQI scores continued to improve in the rocatinlimab groups up to Week 36 and were maintained during the off-treatment period.

Conclusion: Rocatinlimab showed significant improvement in PROs in patients with msAD, which were maintained up to Week 56, suggesting potential disease modifying effects.

Funding: Kyowa Kirin Co., Ltd.

F7

ROCATINLIMAB DEMONSTRATES A SIGNIFICANT REDUCTION IN IgE CONCENTRATIONS IN ADDITION TO CLINICAL EFFICACY MEASURES IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 2B TRIAL

Emma Guttman-Yassky, MD, PhD; Camilla Chong, MD; Ehsanollah Esfandiari, MD, PhD

Introduction: Immunoglobulin E (IgE) plays an important pathogenic role in atopic dermatitis and is elevated in the serum and skin of patients. We investigated the effect of rocatinlimab, an anti-OX40 monoclonal antibody, on serum total IgE concentrations in adult patients with moderate-to-severe atopic dermatitis (msAD).

Methods: This double-blind, placebo-controlled Phase 2b trial (NCT03703102) randomized patients (n=274) 1:1:1:1:1 to subcutaneous rocatinlimab 150 or 600mg every 4 weeks (Q4W) for 36 weeks, 300 or 600mg every 2 weeks (Q2W) for 36 weeks, or placebo (Weeks 0–18; rocatinlimab 600mg Q2W Weeks 18–36), followed by a 20-week off-treatment period (Week 56)(Guttman-Yassky E, et al. Lancet. 2023;401:204-14). The mean percent change from baseline in serum total IgE concentration was evaluated at Weeks 16, 36, and 56.

Results: Overall, 267 patients comprised the full analysis set; rocatinlimab: n=210 (78.7%), placebo: n=57 (21.3%). At Week 16, mean serum total IgE concentrations decreased below baseline across rocatinlimab treatment groups. The reductions continued up to Week 36 and were maintained up to Week 56. In the placebo group, mean serum IgE concentrations increased at Week 16 and decreased below baseline after switching to rocatinlimab 600mg Q2W at Week 18, and further at Weeks 36 and 56. Mean IgE reductions at Weeks 16, 36 and 56 were: –19.7%, –38.9%, –26.7% (150mg Q4W); –17.1%, –39.5%, –46.5% (600mg Q4W); –18.6%, –44.8%, –10.9% (300mg Q2W); –16.9%, –48.6%,–58.5% (600mg Q2W); 34.2%, –8.8%, –29.1% (placebo/600mg Q2W).

Conclusion: The reduction in IgE concentrations is consistent with improvement seen in clinical efficacy endpoints, even during the off-treatment follow-up period, in patients with msAD.

Funding: Kyowa Kirin Co., Ltd.

F8

US patients with chronic rhinosinusitis with nasal polyps enrolled in the AROMA registry have a high burden of disease at baseline regardless of clinician specialty

Larry Borish MD, Jeb M Justice MD, Laurie M McWilliams MD, David W Jang MD

Background: Characteristics and treatment approaches for patients with chronic rhinosinusitis with nasal polyps (CRSwNP) may differ between ear, nose, and throat (ENT) specialists and allergists. AROMA is a prospective global registry of patients initiating dupilumab for CRSwNP in real-world practice.

Methods: Baseline characteristics were assessed according to physician specialty from a planned interim analysis (February 2023) of patients enrolled at US sites in AROMA.

Results: Overall, 115 and 131 patients received care from an ENT specialist and allergist, respectively; 82 patients received care from both specialties. Demographics (mean age 49–50 years, 57–59% female, 76–81% White) were similar across the 3 groups (ENT/allergist/both). Overall, 52–54% had prior surgery; 66% had used oral corticosteroids in the preceding 2 years; and 97–99% had coexisting type 2 diseases. The pattern of standard-of-care assessments was similar across groups: 89–93% of patients were assessed for patient-reported symptoms (Loss of Smell [LoS; range 0–3], Nasal Congestion [NC; 0–3], Total Symptom Score [TSS; 0–9]), and 79–85% for health-related quality of life (22-item Sinonasal Outcome Test [SNOT-22; 0–110]). Mean scores were LoS, 1.9; NC, 1.5–1.7; TSS, 4.7–4.9; SNOT-22, 37–40. Regardless of specialty, other assessments were infrequent, including University of Pennsylvania Smell Identification Test (26–35% of patients), CT scans (8–11%), and biomarkers (eosinophils 10–13%; IgE 12–15%).

Conclusion: Adult patients who initiated dupilumab for CRSwNP in US real-world practice had a consistently high burden of disease across all measures, and had minimal differences in baseline characteristics by specialty, suggesting similar management approaches for ENTs and allergists.

Funding: Regeneron and Sanofi.

F9

Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) had fewer sinus procedures and less healthcare resource utilization (HCRU) after initiating dupilumab in real-world practice

Joseph K. Han, MD; Stella E. Lee, MD; Joshua M. Levy, MD; Zachary M. Soler, MD

Background: This study investigated dupilumab effectiveness in patients with CRSwNP in US real-world practice.

Methods: Retrospective observational cohort study in adults with CRSwNP initiating dupilumab 300 mg between 2019 and 2022 using data from the Reg-ENT^{SM} Registry and the OM1 Real World Data Cloud. HCRU was measured during the 12 months pre- and 12 months post-dupilumab initiation.

Results: 1016 patients were included. In the 12 months post- vs pre-dupilumab initiation, fewer patients had nasal endoscopy (47.5% vs 71.2%), debridement (3.6% vs 9.8%), and CT scan (4.5% vs 22.1%) (all $P<0.001$). Annual mean [SD] number of visits was lower post-initiation vs pre-treatment for outpatient (5.0 [5.2] vs 7.1 [6.0]), including: ambulatory (urgent care or day surgery; 1.2 [2.0] vs 1.9 [2.4]), otolaryngologist (3.7 [6.7] vs 4.0 [6.1]) (all $P<0.001$), and emergency department visits (0.1 [0.6] vs 0.2 [0.6]) ($P<0.05$).

Conclusions: CRSwNP patients on dupilumab had fewer sinus procedures and lower HCRU following dupilumab initiation vs pre-dupilumab treatment. These findings support the effectiveness of dupilumab in treating patients with CRSwNP in real-world practice.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F10

Improved Lung Function is Associated with Better Asthma Control in Adolescents and Adults Aged 12 Years and Older with Moderate-to-Severe Type 2 Asthma: A Post hoc Analysis of QUEST

Brian J. Lipworth, MD; Thomas B Casale, MD; Celeste Porsbjerg, PhD; William W. Busse, MD; Anne K. Ellis, MD; Jérôme Msihid, MSc; Rebecca Gall, MD; Nami Pandit-Abid, PharmD; Zhixiao Wang, PhD; Wei-Han Cheng, PhD; Nicholas Jellots, PharmD; Juby A Jacob-Nara, MD, DHSc; Harry Sacks; MD

Introduction: In LIBERTY ASTHMA QUEST (NCT02414854), add-on dupilumab reduced severe asthma exacerbations and improved lung function and asthma control in adolescents and adults aged with uncontrolled, moderate-to-severe asthma, with an acceptable safety profile. There is inconsistent evidence of a relationship between lung function and asthma symptoms in literature. This post hoc analysis assessed association between lung function improvements and asthma control in QUEST.

Methods: Patients with type-2 asthma (blood eosinophil count ≥150 cells/μL or fractional inhaled nitric oxide ≥25 ppb) were randomized to dupilumab 200 or 300 mg or placebo q2w. Patients were stratified into tertiles based on change from baseline in pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV_1) at Week 52. Lung function responders were defined by pre-BD FEV_1 improvements ≥100 mL or ≥200mL. This study compared proportion of patients with well-controlled asthma (ACQ-5 score ≤0.75) between tertiles and between lung function responders/non-responders in pooled dupilumab and placebo treatment arms.

Results: Mean (SD) change from baseline in pre-BD FEV_1 at Week 52 was −0.15 (0.18), 0.23 (0.10), and 0.81 (0.36) L in low (n=389), medium (n=390), and high (n=391) tertile subgroups, respectively. Greater proportions of patients achieved well-controlled asthma in high-tertile subgroup (44.8% compared with low-tertile subgroup (21.6%, odds ratio [OR] high versus (vs) low-tertile 3.30; [95% CI] [2.34, 4.65], P<0.0001),54.3% and 45.7% of patients achieved improvement from baseline pre-bronchodilator FEV_1 of ≥100 mL and ≥200 mL at Week 52, respectively. Greater proportions of responders achieved well-controlled asthma at Week 52 (≥100mL responders vs non-responders 39.2% vs 15.1%, OR 3.94, [2.97, 5.22]; ≥200mL responders vs non-responders 40.5% vs 18.0%, OR 3.39, [2.60, 4.42]; P<0.0001 for both).

Conclusion: Lung function improvement and meeting lung function response thresholds were associated with better asthma control in patients with uncontrolled moderate-to-severe type 2 asthma in pooled dupilumab and placebo treatment arms.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F11

Dupilumab Treatment Shows Consistent Improvement in Atopic Dermatitis in All Anatomical Regions in Patients Aged 6 Months to 17 Years: Results From an Open-Label Extension Study

Elaine C. Siegfried, MD; Eric L. Simpson, MD; Michael J. Cork, PhD; Hidehisa Saeki, PhD; Zhen Chen, MBA, PhD; Elizabeth Simcox, PhD; Randy Prescilla, MD*.

Background: This analysis reports the impact of dupilumab treatment on atopic dermatitis (AD) signs across anatomical regions in patients aged 6 months to 17 years with AD in an open-label extension (OLE) study.

Methods: This ongoing, Phase 3 OLE (NCT02612454) enrolled patients aged 6 months to 17 years with moderate-to-severe AD who received a weight-tiered dupilumab regimen every 4 weeks (200 mg: 5 to <15 kg; 300 mg: 15 to <30 kg) or every 2 weeks (200 mg: 30 to <60 kg). This interim analysis reports unweighted Eczema Area and Severity Index (EASI) body region scores across anatomical regions (range 0–12) at baseline and Week 52.

Results: At baseline, 180 patients were included in the 6 months to 5 years group, 368 in the 6–11 years group, and 275 in the 12–17 years group. Unweighted mean (standard deviation [SD]) EASI body regions scores decreased in all anatomical regions in the 6 months to 5 years group (baseline/Week 52): head, 5.1 (3.2)/1.7 (1.9); trunk, 4.4 (3.2)/1.5 (2.0); upper extremities, 6.5 (3.5)/2.4 (2.7); lower extremities, 6.7 (3.4)/2.8 (2.6). Similar improvement was observed in the 6–11 years group: head, 4.3 (3.3)/1.7 (1.9); trunk, 3.6 (3.5)/1.2 (1.7); upper extremities, 6.0 (3.3)/3.0 (2.6); lower extremities, 6.0 (3.5)/2.8 (2.7); and in the 12–17 years group: head, 4.8 (3.1)/2.1 (2.3); trunk, 5.0 (3.3)/1.5 (2.2); upper extremities, 6.9 (3.2)/4.0 (3.2); lower extremities, 6.9 (3.4)/2.6 (2.9).

Conclusion: Dupilumab treatment provides sustained improvement in AD signs across all anatomical regions in children aged 6 months to 17 years with moderate-to-severe AD.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F12

Children With Atopic Dermatitis Respond More Rapidly to Dupilumab Treatment in Comparison to Adolescents and Adults

Evgeny Berdyshev, PhD; Elena Goleva, PhD; Simon G. Danby, PhD; Anna S. Bronoff, BSc; Inoncent Agueusop, PhD; Joseph Zahn, MD; Emilie Gloaguen, PhD; Robert Bissonnette, MD; Mark Boguniewicz, MD; Peck Ong, MD; Annie Zhang, MD*; Michael J. Cork, PhD; Donald Y. M. Leung, PhD, MD.

Introduction: Dupilumab, a monoclonal antibody that inhibits interleukin (IL)-4 and IL-13, is used to treat moderate-to-severe atopic dermatitis (AD) across the age span from 6 months and older.

Methods: We assessed the skin of AD patients of the 6−11 years (PELISTAD study (NCT04718870), n=23) versus 12−65 years (BALISTAD study [NCT04447417], n=26) age groups during 16 weeks of dupilumab treatment. Eczema Area and Severity Index (EASI) score and lipids from stratum corneum collected by skin tape stripping (STS) were evaluated longitudinally.

Results: There were no differences in EASI scores between the 6−11 and 12−65 year age groups at baseline (Mean±SE: 34.85±2.55 vs 31.18±3.25, respectively). Dupilumab treatment resulted in more rapid improvement in EASI scores in the 6−11 as compared to 12−65 age group (Mean±SE week 3 of treatment: 11.97±2.14 vs 19.52±2.96 (P=0.027), Week 8: 9.76±2.26 vs 13.48±2.16 (P=0.022) for these age groups, respectively). Lipid STS analysis at Week 8 revealed that in the 6−11 age group, in the lesional skin, the omega esterified fatty acid sphingosine (EOS) ceramides (CER) nearly achieved the levels of EOS CER in healthy skin (91% improvement), compared to 45% improvement in the 12−65 year age group. The levels of N(C22) S-ceramides in AD lesional skin improved 52.9% in the 6−11 age group compared to 32% in the 12−65 age group at Week 8, respectively.

Conclusion: Our data shows that in the younger age group dupilumab intervention results in more rapid significant improvement in clinical severity, and normalization of barrier lipids, suggesting that early intervention may provide better treatment outcomes for skin barrier lipids and disease severity in AD.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F13

Understanding the Impact of Long-Term Prophylaxis Switches for Patients With Hereditary Angioedema

Steve Dorman, MD, Donald L. McNeil, MD, Jean A. Nelson, MD, Lucy Howard, BSc, Will Ambler, PhD, Tom Bailey, MSci, Daniel Fox, PharmD, MBA, Krystal Sing, PharmD, Bob G. Schultz, PharmD, MS, Salomé Juethner, MSN

Introduction: Data on the impact of long-term prophylaxis (LTP) treatment switches on disease management and patient-reported outcomes (PROs) in adult patients with hereditary angioedema (HAE) are limited.

Methods: A non-interventional, observational, multicenter chart review and site-/patient-level survey was conducted. Adult patients (aged >18 years) with HAE residing in the US who initiated LTP treatment with lanadelumab before switching to berotralstat then back to lanadelumab, were eligible for enrollment. Clinical and PRO data were collected.

Results: Six patients were included for interim analysis (mean±SD age, 49.7±17.9 years; 100% female; 50.0% Type I HAE; 33% normal C1-inhibitor HAE). Mean±SD time on each treatment cycle was 38.5±10.5 months, 5.4±9.0 months, and 8.9±13.9 months (lanadelumab>berotralstat>lanadelumab). Reasons for discontinuing lanadelumab (first cycle) included patient request (33%), clinical trial enrollment (33%), financial/co-pay (17%), and poor tolerability (17%); no patients discontinued due to lack of effectiveness. Patients discontinued berotralstat due to lack of effectiveness (67%; defined as “attack frequency/severity was not reduced adequately” and “did not achieve attack-free status”) and poor tolerability (50%). No patients reported severe/life-threatening HAE attacks while on either lanadelumab cycle, while 50% of patients experienced severe/life-threatening attacks using berotralstat. Most patients (66%) were ‘completely satisfied’ with lanadelumab on both treatment cycles, whereas no patients were ‘completely satisfied’ with berotralstat treatment.

Conclusions: Albeit an early interim analysis with ongoing data collection, most patients who switched from lanadelumab>berotralstat>lanadelumab cited lack of effectiveness as the reason for switching and most reported complete satisfaction with lanadelumab. Given the selection criteria, these findings should not be extrapolated to all patients with HAE.

Funding: Takeda Pharmaceuticals USA, Inc.

F14

Lanadelumab Effectiveness and Safety in Adolescent Patients With Hereditary Angioedema Aged 12 to <18 Years: Pooled Results From the Real-World ENABLE and EMPOWER Studies

Raffi Tachdjian, MD, Aleena Banerji, MD, Paula J. Busse, MD, Nancy Agmon-Levin, Professor, John Anderson, MD, Mauro Cancian, MD, Giuseppe Spadaro, Professor, Carmen Enciu, MD, Daniel Nova Estepan, PharmD, Natalie Khutoryansky, PhD, Andreas Recke, MD

Introduction: Data on long-term prophylaxis outcomes in adolescents with hereditary angioedema (HAE) are scarce. This analysis assessed lanadelumab treatment outcomes in adolescents with HAE using pooled data from the real-world Phase IV ENABLE (NCT04130191) and EMPOWER (NCT03845400) studies.

Methods: Adolescents (12–<18 years) with HAE Type I/II from ENABLE and EMPOWER were included. Outcomes were analyzed in new (lanadelumab-naïve; <4 lanadelumab doses before enrollment) and established (≥4 lanadelumab doses before enrollment) lanadelumab users.

Results: Overall, 13 new (mean±SD age: 15.2±2.03 years, mean±SD weight: 77.4±32.26 kg, female: 53.8%, HAE Type I: 76.9%) and 7 established (mean±SD age: 15.7±1.38 years, mean±SD weight: 87.8±34.81 kg, female: 71.4%, HAE Type I: 85.7%) adolescent lanadelumab users were included; all patients were White. HAE attack rate in new users decreased by 63.0% post-lanadelumab, from 1.66 (95% CI 0.97–2.82) attacks/month at baseline (ENABLE: pre-lanadelumab, EMPOWER: pre-enrollment) to 0.61 (95% CI 0.30–1.22) attacks/month post-lanadelumab (incidence rate ratio [IRR] 0.37, 95% CI 0.15–0.89), and by 73.0% during lanadelumab steady state (IRR 0.27; 95% CI 0.10–0.72). In established users, HAE attack rate as treated (mean±SD) during the overall study period was 0.1±0.13 attacks/month. Most HAE attacks were mild/moderate, treated with on-demand medications (most frequently C1 inhibitors or icatibant) and did not require visits to healthcare professionals. There were 34 treatment-emergent adverse events (TEAEs; mild/moderate:85.3%, non-serious:91.2%) in 9/13 new and 7 TEAEs (all mild/moderate and non-serious) in 5/7 established users. No TEAEs were related to lanadelumab.

Conclusions: Data from real-world settings suggest sustained lanadelumab safety and effectiveness in adolescents, similar to results from pivotal studies in mixed adult/adolescent populations.

Funding: Takeda Development Center Americas, Inc.

F15

Effect of tezepelumab in patients with severe, uncontrolled asthma by age of onset, allergic status, and eosinophilic phenotype

Sameer K Mathur, Jennifer L Hill, Christopher S Ambrose, Nicole Martin, Jean-Pierre Llanos, Neil Martin, Gene Colice

Introduction: Biologic efficacy for severe asthma varies depending on age of asthma onset and inflammatory phenotype. This *post hoc* analysis assessed the effect of tezepelumab in patients with severe, uncontrolled asthma with childhood-onset and current allergic or non-eosinophilic disease and adult-onset and current eosinophilic or non-allergic disease using pooled data from the phase 2b PATHWAY and phase 3 NAVIGATOR studies.

Methods: PATHWAY (NCT02054130) and NAVIGATOR (NCT03347279) were multicenter, randomized, placebo-controlled studies with similar designs. Included patients (12–80 years old) received tezepelumab 210 mg or placebo subcutaneously every 4 weeks for up to 52 weeks. Annualized asthma exacerbation rates (AAERs) over 52 weeks were assessed in patients grouped by age of asthma onset (childhood-onset, <18 years; adult-onset, ≥18 years) in combination with inflammatory phenotype (non-eosinophilic, baseline blood eosinophil count [BEC] <150 cells/μL; eosinophilic, baseline BEC ≥150 cells/μL; or allergy to a perennial aeroallergen [positive/negative serum specific immunoglobulin E test]). Subgroups were not mutually exclusive.

Results: Tezepelumab reduced the AAER over 52 weeks versus placebo by 53% (95% CI: 34–67) in patients with childhood-onset, allergic asthma (tezepelumab, n=181; placebo, n=180); 49% (95% CI: 9–72) in patients with childhood-onset, non-eosinophilic asthma (tezepelumab, n=58; placebo, n=57); 67% (95% CI: 57–74) in patients with adult-onset, eosinophilic asthma (tezepelumab, n=330; placebo, n=332); and 54% (95% CI: 37–67) in patients with adult-onset, non-allergic asthma (tezepelumab, n=198; placebo, n=204).

Conclusions: Tezepelumab reduced exacerbations versus placebo in a broad population of patients with severe, uncontrolled asthma grouped by age of onset and inflammatory phenotype.

Funding: AstraZeneca and Amgen Inc.

F16

Tezepelumab efficacy in dupilumab-eligible patients: a pooled analysis from the PATHWAY and NAVIGATOR studies

Marco Caminati, Andrew W Lindsley, Joseph D Spahn, Bill Cook, Gillian Hunter and Jean-Pierre Llanos

Introduction: Tezepelumab, a human monoclonal antibody, blocks the activity of thymic stromal lymphopoietin (TSLP). In the phase 2b PATHWAY (NCT02054130) and phase 3 NAVIGATOR (NCT03347279) studies, tezepelumab reduced exacerbations and improved lung function, asthma control and health-related quality of life versus placebo in patients with severe, uncontrolled asthma. This pre-specified exploratory analysis evaluated the efficacy of tezepelumab in patients pooled from the PATHWAY and NAVIGATOR studies, according to dupilumab treatment eligibility (EU prescribing information).

Methods: PATHWAY and NAVIGATOR were multicenter, randomized, double-blind, placebo-controlled, parallel-group studies with similar designs. Patients (12–80 years old) with severe, uncontrolled asthma who received tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks were included in the pooled population. For this exploratory analysis, dupilumab eligibility was defined as having type 2-high asthma with baseline fractional exhaled nitric oxide (FeNO) levels ≥25 ppb and/or baseline blood eosinophil counts (BECs) ≥150 cells/μL, with inadequately controlled asthma despite high-dose inhaled corticosteroids plus an additional controller medication. The annualized asthma exacerbation rate (AAER) over 52 weeks and the change from baseline to week 52 in pre-bronchodilator (BD) forced expiratory volume in 1 second (FEV_1) were assessed in dupilumab-eligible patients.

Results: Overall, 800 patients (tezepelumab, n=395; placebo, n=405) were dupilumab-eligible. In these patients, tezepelumab reduced the AAER over 52 weeks versus placebo by 66% (95% confidence interval [CI]: 58–73). At week 52, improvements in pre-BD FEV_1 were greater with tezepelumab than placebo (least-squares mean change from baseline, 0.28 L vs 0.08 L; difference 0.20 [95% CI: 0.14–0.26] L). Clinically meaningful improvements in pre-BD FEV_1 were evident from week 4 (first measurement time point in PATHWAY) in tezepelumab-treated patients.

Conclusions: Tezepelumab reduced exacerbations and improved pre-BD FEV_1 versus placebo in dupilumab-eligible patients, supporting the benefits of tezepelumab in patients with type 2-high, severe, uncontrolled asthma

Funding: AstraZeneca and Amgen, Inc.

F17

Clinical responses to tezepelumab in patients with severe, uncontrolled asthma and a history of chronic rhinosinusitis with nasal polyps from the NAVIGATOR study

Njira L Lugogo, Anju T Peters, Geoffrey L Chupp, Michael E Wechsler, Scott Caveney, Nicole Martin, Bhavini Parikh and Christopher S Ambrose

Introduction: In the phase 3 NAVIGATOR (NCT03347279) study, tezepelumab improved asthma outcomes and sino-nasal symptoms versus placebo in patients with severe asthma and a history of chronic rhinosinusitis with nasal polyps (CRSwNP). This *post hoc* analysis compared the effect of tezepelumab versus placebo on clinical response in NAVIGATOR patients with severe, uncontrolled asthma and a history of CRSwNP.

Methods: NAVIGATOR was a multicenter, randomized, double-blind, placebo-controlled study. Patients (12–80 years) were randomized to tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. The proportions of patients with a history of CRSwNP who achieved clinical responses at week 52 were assessed. Clinical response criteria included: a decrease from baseline in Asthma Control Questionnaire-6 total score of ≥0.5; an increase in pre-bronchodilator FEV_1 ≥100 mL or ≥5%; a ≥50% reduction in exacerbations from the previous year; a Clinical Global Impression of Change score defined as minimally, much or very much improved; and a decrease in Sino-Nasal Outcome Test-22 total score ≥8.9. Complete response was defined as when all five criteria were met.

Results: Overall, 165 patients had a history of CRSwNP (tezepelumab, n=90; placebo, n=75). At week 52, a higher proportion of tezepelumab than placebo recipients in the on-treatment population met clinical response criteria and achieved a complete response (31% vs 11%; OR: 5.65 [95% CI: 1.83–17.51]). Findings were similar when patients who did not complete the planned treatment period or had missing data were included and treated as non-responders (OR: 4.41 [95% CI: 1.53–12.68]).

Conclusions: Among patients with severe, uncontrolled asthma and a history of CRSwNP, greater proportions of tezepelumab than placebo recipients achieved on-treatment clinical responses. Nearly one-third of tezepelumab recipients achieved complete response. These data further support the efficacy of tezepelumab in patients with severe, uncontrolled asthma and a history of CRSwNP.

Funding: AstraZeneca and Amgen Inc

F18

Effect of Dupilumab Treatment on Mucus Plugging and Mucus Volume in Type 2 Asthma: The Phase 4 VESTIGE Trial

Celeste Porsbjerg, PhD; Eleanor M Dunican, PhD; Njira L. Lugogo MD, Mario Castro, MD; Alberto Papi, MD; Vibeke Backer, MD DMSci; Christopher E. Brightling, PhD; Arnaud Bourdin, MD; J. Christian Virchow, MD; Mei Zhang, PhD; Xavier Soler, MD; Nicholas Jellots*, PharmD; Paul J. Rowe, MD; Yamo Deniz, MD; Lucía de Prado Gómez, PhD; Harry Sacks, MD; Juby A. Jacob-Nara, MD

Introduction: Mucus hypersecretion resulting from chronic airway inflammation is a key driver of intermittent airway obstruction and airway remodeling in patients with asthma. Dupilumab blocks the shared receptor component for IL-4/IL-13, and has been shown to improve lung function and reduce rate of severe exacerbations in patients with moderate-to-severe asthma. VESTIGE study (NCT04400318) assessed the impact of dupilumab treatment on airway inflammation and structural airway changes in patients with asthma.

Methods: Patients aged 21-70 years (with uncontrolled moderate-to-severe asthma and elevated type 2 biomarkers, pre-bronchodilator percent predicted forced expiratory volume in 1 second (pre-BD ppFEV_1) ≤80%, and ≥1 exacerbation in the year prior, were randomized 2:1 to add-on dupilumab 300 mg (n=72) or matched placebo (n=37) every 2 weeks for 24 weeks. Proportion of patients achieving FeNO <25 ppb and least squares (LS) mean change in pre-BD FEV_1 at Week 24, was assessed.

Results: At Week 24, patients treated with dupilumab had reduced airway mucus scores (LS mean difference [standard error, SE] from baseline was -4.9 [0.8] points vs placebo; nominal P<0.001) and reduced airway mucus volumes (−0.107 [0.020] mL vs placebo; nominal P<0.001). Patients receiving dupilumab were 9.8 times more likely to achieve FeNO <25 ppb by Week 24 than those on placebo (P<0.001). An improvement in pre-BD FEV_1 was observed at Week 24 (LS mean difference [SE] vs placebo: 0.38 [0.11] L; nominal P<0.001). Furthermore, improvements from baseline to Week 24 in pre-BD FEV_1 were strongly associated with decreases in airway mucus scores in dupilumab-treated patients (Pearson's correlation coefficient −0.618; P<0.0001).

Conclusion: Dupilumab treatment led to a significant reduction in mucus airway plugging and mucus volume, as well as reduction in airway inflammation, contributing to improvements in lung function.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F19

Dupilumab Reduces Disease Activity in Patients with Chronic Spontaneous Urticaria: LIBERTY-CSU CUPID Study A

Marcus Maurer, MD; Ana Giménez-Arnau, PhD; Allen Kaplan, MD; Sarbjit Saini, MD; Luis Felipe Ensina, PhD; Michihiro Hide, PhD; Amy Praestgaard, MS; Tayler Gonzalez, Pharm D; Sonya Cyr,PhD; Philip Sugerman, PhD

Introduction: Chronic spontaneous urticaria (CSU) is a chronic inflammatory disease characterized by wheals and/or angioedema that recur for >6 weeks. The overall goal of CSU treatment is to clear the signs and symptoms until urticaria shows spontaneous remission. Many patients with CSU fail to respond adequately to standard-of-care H1-antihistamines (H1-AH).

Methods: LIBERTY-CSU CUPID Study A (NCT04180488) was a randomized, placebo-controlled, 24-week, phase 3 trial that evaluated dupilumab efficacy and safety in patients aged ≥6 years with CSU who remained symptomatic despite H1-A1 treatment and were omalizumab-naïve. Background therapy was study-defined H1-AH at up to 4-fold the approved dose. Endpoints included the proportion of patients with Urticaria Activity Score over 7 days (UAS7) ≤6 and UAS7=0 up to Week 36.

Results: In patients with CSU inadequately controlled with H1-AH, dupilumab treatment resulted in a numerically greater proportion of patients achieving well-controlled urticaria (UAS76) from Week 8 and urticaria-free status (UAS7=0) status from Week 14, vs placebo. At Week 24, 53.1% of dupilumab-treated patients achieved UAS7≤6 and 35.9% achieved UAS7=0 (vs 34.0% and 18.9% with placebo; P=0.0379 and P=0.0411, respectively). Following discontinuation of dupilumab at Week 24, the proportion of patients achieving well-controlled urticaria (UAS7≤6) or urticaria-free status (UAS7=0) status remained numerically greater for dupilumab vs placebo to Week 36.

Conclusion: A numerically greater proportion of patients treated with dupilumab achieved well-controlled urticaria (UAS≤6) or urticaria-free status (UAS7=0) status vs placebo. Dupilumab safety was consistent with the known safety profile.

Funding: Sanofi and Regeneron Pharmaceuticals Inc.

F20

Long-term safety and efficacy with garadacimab for hereditary angioedema prophylaxis in an open-label extension study

John Anderson, MD; Donald S Levy, MD; Gordon L Sussman, MD; Joshua S Jacobs, MD; Henriette Farkas, MD, PhD; Maressa Pollen, MD*; Henrike Feuersenger, PhD; Timothy J Craig, DO

Introduction: Hereditary angioedema (HAE) causes recurrent, debilitating attacks. Prophylaxis with garadacimab (CSL312, anti-activated factor XII monoclonal antibody) demonstrated efficacy with a favorable safety profile in double-blind Phase 2 and pivotal Phase 3 (VANGUARD) studies. We report results from an ongoing open-label extension (OLE) study (NCT04739059).

Methods: Patients received garadacimab 200 mg subcutaneously once-monthly. The primary endpoint was treatment-emergent adverse events (TEAEs) in patients with HAE due to C1 esterase inhibitor deficiency (HAE-C1-INH). Secondary endpoints included monthly number of attacks and reduction in monthly number of attacks vs run-in.

Results: The overall patient population (N=161) comprised Phase 2 roll-over (n=35), pivotal Phase 3 roll-over (n=57, including 21 previously receiving placebo), and newly enrolled patients (n=69). As of February 2023, median (interquartile range) garadacimab exposure was 13.8 months (11.9–16.3), and 119/161 patients (73.9%) had ≥12 months' garadacimab exposure. Of 159 patients (safety analysis set), 133 (83.6%) experienced ≥1 TEAE. Most TEAEs (510/524, 97.3%) were mild/moderate. TEAEs experienced by ≥10% of patients were coronavirus disease 2019 (57/159 patients, 35.8%), nasopharyngitis (27/159, 17.0%), and injection-site reactions (19/159, 11.9%). Three serious TEAEs (all unrelated to garadacimab) occurred. No TEAEs of special interest defined per protocol occurred (thromboembolic events, abnormal bleeding events, severe hypersensitivity including anaphylaxis). Mean (standard deviation) monthly number of attacks was 0.16 (0.37) during garadacimab vs 3.57 (2.41) during run-in, corresponding to a 94.7% (12.0) reduction. Consistent percentages of attack-free patients were observed over time across treatment windows.

Conclusion: Consistent with Phase 2 and 3 studies, garadacimab demonstrated a favorable safety profile in the long term, accompanied by durable efficacy.

Funding: CSL Behring

F21

Long-term efficacy and safety of subcutaneous garadacimab for prophylaxis of hereditary angioedema attacks: Results from the open-label extension of a multicentre phase 3 study

Markus Magerl, MD; Avner Reshef, MD; Henriette Farkas, MD, PhD; H Henry Li, MD*; Joshua S Jacobs, MD; Jonathan A Bernstein, MD; William H Yang, MD; Erik S G Stroes, PhD; Isao Ohsawa, MD; Raffi Tachdjian, MD; Michael E Manning, MD; William R Lumry, MD; Inmaculada Martinez Saguer, MD; Emel Aygören-Pürsün, MD; Bruce Ritchie, MD; Gordon L Sussman, MD; John Anderson, MD; Kimito Kawahata, MD; Yusuke Suzuki, MD; Petra Staubach, MD; Regina Treudler, MD; Henrike Feuersenger, PhD; Iris Jacobs, MD; Timothy J Craig, DO

Introduction: The safety and efficacy of garadacimab (CSL312, anti-activated factor XII monoclonal antibody) were evaluated in a pivotal, randomised, placebo-controlled, multicentre, Phase 3 trial and an open-label extension (OLE) trial.

Methods: Patients aged ≥12 years with type I/II hereditary angioedema (HAE) (N=64) received monthly subcutaneous (SC) garadacimab 200 mg (n=39) or placebo (n=25) for 6 months after an initial 400 mg SC loading dose or matched placebo. Primary and key secondary endpoints of the Phase 3 trial and the long-term efficacy and safety of garadacimab in patients who rolled over into the OLE (n=57) are reported.

Results: Garadacimab significantly reduced mean number of investigator-confirmed HAE attacks per month (0.27 [95% confidence interval {CI} 0.05, 0.49]) vs placebo (2.01 [1.44, 2.57]; P<0.001). Of garadacimab-treated patients, 24 (61.5%) were attack-free and 29 (74.4%) achieved ≥90% attack reduction vs run-in period; no patients in placebo arm were attack-free and two (8.3%) achieved ≥90% attack reduction vs run-in period. Interim OLE data (as of 30/09/2022) show that efficacy of garadacimab (n=36) was sustained; mean (median; CI) reduction in time normalised number of HAE attacks was –95.8% (–100.0%; –100.0, –91.6) vs run-in period. In the Phase 3 trial, safety profiles of both groups were similar. Coronavirus disease 2019 was the most common treatment emergent adverse event (AE) in the OLE. One severe serious AE (laryngeal attack) assessed as not related to trial treatment. No AEs of special interest per protocol, deaths or treatment discontinuations due to AEs were observed. In the OLE, safety profiles were consistent with Phase 3 trial data.

Conclusions: Once-monthly SC garadacimab substantially reduced the number of HAE attacks vs placebo with early onset of protection from first dose, sustained efficacy beyond 12 months, and a favourable safety profile. Efficacy in the OLE was comparable between both groups.

Funding: CSL Behring

F22

Early onset of protection against hereditary angioedema attacks from Week 1 with garadacimab in pivotal Phase 3 (VANGUARD) study

Raffi Tachdjian, MD; H Henry Li, MD, PhD*; Connie Hsu, MD; Roman Hakl, PhD; Petra Staubach, MD; Lolis Wieman, PhD; John-Philip Lawo, MSc; Paul Keith, MD

Introduction: Hereditary angioedema (HAE) causes recurrent, unpredictable, and potentially life threatening attacks associated with significant disease burden. Garadacimab (CSL312, anti activated factor XII monoclonal antibody) significantly reduced the monthly number of attacks vs placebo (mean, 87%; median, 100%; P<0.0001) with favorable tolerability and safety profile in a pivotal Phase 3 study (VANGUARD). Early onset of treatment effect and durability are critical for improving HAE control and decreasing disease burden. This post hoc analysis reports early onset and durability of efficacy of garadacimab.

Methods: Following run-in, patients aged ≥12 years with HAE due to C1 esterase inhibitor deficiency (HAE-C1-INH) were randomized (3:2) to garadacimab 200 mg subcutaneous once monthly after an initial 400 mg loading dose (n=39) or volume-matched placebo (n=25).The monthly number of attacks and percentage of attack-free patients at weekly (Weeks 1–4) and monthly (Months 1–6) intervals were calculated.

Results: Garadacimab substantially reduced the mean monthly number of attacks (95% confidence interval [CI]) as early as Week 1 vs run-in (0.11 [-0.11–0.34] vs 3.07 [2.41–3.73], respectively), unlike placebo (1.81 [0.74–2.88] vs 2.52 [2.13–2.91], respectively). Mean monthly number of attacks remained consistently lower with garadacimab vs both run-in and placebo throughout the study (Weeks 1–4 and Months 1–6). The percentage of attack-free patients was higher at Weeks 1–4 for garadacimab (92.3–97.4%) vs placebo (50.0–66.7%) and remained consistently higher at Months 1–6 (76.9–89.7%) vs placebo (9.1–36.4%).

Conclusion: Garadacimab provides early onset and durable efficacy in the reduction and prevention of HAE attacks from as early as Week 1.

Funding: CSL Behring

F23

Trends in volume of on-demand hereditary angioedema treatments in the US: A retrospective analysis of a large multi-payer claims database

Daniel F. Soteres, Chirag Maheshwari, Abhishek Sharma, Alice Wang, Paul K. Audhya, Raffi Tachdjian

Introduction: Management of hereditary angioedema (HAE) is comprised of two main pharmacological strategies: effective on-demand treatment of attacks and the addition of long-term prophylaxis (LTP) in appropriate patients. Since 2017, the use of subcutaneous and oral LTP treatments has grown substantially. Real-world data on utilization of on-demand treatments in years following the introduction of these agents is limited.

Methods: Patients from the IQVIA PharMetrics® Plus Database records (Q3 2018 – Q3 2023) were included. Eligible patients had ≥1 claim for approved HAE-specific on-demand treatment (specific indication not available). Descriptive analyses of total number of claims reimbursed and quantity dispensed per quarter were described.

Results: A total of 1,706 patients were identified. Mean (SD) age was 45 (16.8) years, 66% female, 44% live in the South, 23% Midwest, 18% West and 15 % Northeast. The total number of patients with on-demand claims declined from 314 in Q3 2018 to 257 in Q4 2020 but climbed back to 312 in Q2 2023. On average, 291 patients were dispensed on-demand HAE treatments per quarter, with an average of 592 claims reimbursed per quarter. Icatibant accounted for about 61% of the total claims, 15% plasma-derived C1 esterase inhibitor (pdC1-INH), 17% recombinant C1 esterase inhibitor (rhC1-INH), and 7% ecallantide. On average, 21 vials of rhC1-INH per patient per quarter were dispensed, 18 vials of pdC1-INH, 24 vials of ecallantide, and 7 syringes of icatibant. Total quantity dispensed has been broadly stable during the analysis period, with an average year-over-year change in the total number of syringes and vials dispensed per quarter within 3% and 10%, respectively.

Conclusions: Despite the advent of multiple non-androgen LTPs since 2017, the overall trend in the total number of claims reimbursed and quantity dispensed for on-demand treatments has remained stable.

Funding: KalVista Pharmaceuticals

F24

Healthcare costs among commercially-insured patients with hereditary angioedema managed with long-term prophylaxis: A retrospective US claims database analysis

Raffi Tachdjian MD, Daniel F. Soteres, MD, Rose Chang ScD, Manasi Mohan MS, Megan Pinaire MPH, Maral DerSarkissian PhD, Vibha Desai PhD, Alice Wang MA, Paul Audhya MD

Introduction: Management of hereditary angioedema (HAE) consists of on-demand treatment and, for appropriate patients, the addition of long-term prophylaxis (LTP). Given the increasing number of patients receiving non-androgen LTP and limited data on related real-world healthcare costs in the US, we estimated such costs based on a large retrospective insurance claims database.

Methods: Eligible commercially-insured patients from the IQVIA PharMetrics® Plus Database records (April 2017 to March 2022) had ≥1 claim for non-androgen LTPs (lanadelumab, berotralstat, intravenous [IV] C1 esterase inhibitor [C1INH] and subcutaneous [SC] C1INH), were ≥12 years old at index (i.e., first non-androgen LTP claim), had ≥6 months of continuous enrollment before and ≥3 months following index. Descriptive analyses examined HAE-related healthcare costs (per patient per year [PPPY]) associated with outpatient visits (OP), inpatient admission (IP), emergency department visit (ED), and home healthcare visits (HH).

Results: The analytic cohort consisted of 210 individuals with a mean ± standard deviation (SD) age of 41±14 years, 72% female, and median follow-up of 16 months. The most common non-androgen LTP treatment received was lanadelumab (50%) followed by SC C1INH (34%), IV C1INH (8%), and berotralstat (8%). Mean total HAE-related healthcare costs PPPY were $641,166. Mean HH costs for patients with at least one HH visit (22%) were $207,784. Mean IP costs for patients with at least one IP visit (11%) were $30,061. Among patients with at least one ED visit (33%), mean costs of ED visits were $25,606. Mean OP costs were $3,297 for patients with at least one OP visit (90%).

Conclusions: While LTP therapies have been shown to reduce HAE attack rates, analyses revealed that HAE-related non-pharmacy resource utilization costs were substantial in the current study. Future insights related to HAE attack management and cost drivers are needed among LTP users.

Funding: KalVista Pharmaceuticals

F25

neffy, epinephrine nasal spray, Demonstrates a Positive Efficacy and Safety Profile for the Treatment of Allergic Reactions in Pediatric Patients at-Risk of Anaphylaxis: Phase 3 Study Results

Motohiro Ebisawa, MD, PhD, Kento Takahashi, MD, Kyohei Takahashi, MD, PhD, Noriyuki Yanagida, MD, PhD, Sarina Tanimoto MD, PhD

Introduction: neffy (epinephrine nasal spray) is being developed as a needle-free option for the treatment of severe allergic reactions. neffy has well-established pharmacokinetic and pharmacodynamic profiles that are within range of approved epinephrine injection products, however there are ethical and practical barriers limiting efficacy studies in patients experiencing severe allergic reactions. The current study assessed the neffy's efficacy in patients who developed anaphylactic symptoms after oral food challenge (OFC).

Methods: In this Phase 3 study (jRCT2031230143), the efficacy and safety of a single dose of neffy (1.0mg in patients 15 to <30 kg and 2.0mg in patients with ≥ 30 kg) was assessed in pediatric patients with allergy symptoms induced by an OFC. neffy was dosed when patients exhibited gastrointestinal, respiratory, or circulatory symptoms that were Grade 2 or higher according to the Severity Classification of Organ Symptoms by the Japanese Society of Allergology Anaphylaxis Guidelines 2022.

Results: The study included 15 patients (n=6 for 1 mg and n=9 for 2 mg) aged 6 - 17. A total of 18 Grade 2 symptoms were observed. No patients needed a second dose of epinephrine within 15 minutes post-dose. One patient had a biphasic reaction 2h and 45 min after initial neffy dosing and required additional epinephrine treatment. The median time to symptom resolution was 16 min (range of 1 - 90 min). Seven patients exhibited adverse events, all which were mild or moderate and mostly resolved quickly.

Conclusions: neffy appears to be an effective needle-free option for the treatment of anaphylactic symptoms.

Funding: ARS Pharma, Inc

F26

Insights Into APDS: Revealing the Patient Experience

Kristie Cline, MBA; Erin Slattery; Michelle Slattery

Introduction: Patient perspectives are essential in improving health outcomes, from drug development through access to care. Patient and caregiver advisory meetings provided insights into living with Activated PI3K Delta Syndrome (APDS), disease management and community needs.

Methods: Two virtual advisory meetings were conducted in 2023, one with 7 patients (6 women, 1 man), ages 20 - 51, living with APDS, and one with 6 caregivers (mothers, ages 39-58) of people living with APDS, ages 17-35. The meetings included polls, a chatroom, and live illustration.

Results: Participants' experiences with APDS are collated into 3 themes below:

1. Disease understanding. Misdiagnoses delayed the pathway to proper care. Family members are often reluctant to undergo genetic testing for APDS due to stigma and misinformation. Some APDS-related symptoms were unknown to patients, despite access to resources and healthcare providers familiar with APDS.
2. Daily living. Fatigue and brain fog are not commonly reported APDS symptoms in published-literature. However, both patients and caregivers reported fatigue as the biggest challenge and associated with brain fog. Infection risks led many to live in a "bubble." These factors impact school and work. Caregivers are concerned about their child's future ability to live independently; nearly all ~~their~~ adult children with APDS live at home.
3. Support system. All patients reported a desire for more emotional/mental health support. Caregivers said frequent illnesses impact their child's mental health, while they struggle with their own physical and mental health. None had met other APDS patients or caregivers prior to the meetings; all wanted opportunities to connect with the APDS community.

Conclusions: These meetings revealed a need for patient-friendly resources for those diagnosed with APDS, psychosocial support, and caregiver resources. Additional research is suggested to assess the prevalence of fatigue and brain fog in those living with APDS.

Funding: Pharming Healthcare, Inc

F27

Initial Results from Summit: An On-going, 3-Part, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Study of Bezuclastinib in Adult Patients with NonAdvanced Systemic Mastocytosis (NonAdvSM)

Jay Chatfield, PhD; Brian D. Modena, MD; Cem Akin, MD, PhD; Mariana Castells, MD; and Prithviraj Bose, MD

Introduction: Bezuclastinib (CGT9486) is an oral, potent, and selective type 1 tyrosine kinase inhibitor with demonstrated clinical activity and acceptable tolerability in the advanced forms of systemic mastocytosis (SM). However, the vast majority of patients with SM have Non-Advanced SM (NonAdvSM).

Methods: Summit (NCT05186753) is a Phase 2, 3-Part, randomized, double-blind, placebo-controlled clinical trial of bezuclastinib in patients with NonAdvSM and inadequate symptom control despite best supportive care (BSC). In Part 1 (Part 1a+1b), patient-reported outcomes assess symptoms and HRQoL in ~50 patients randomized 1:1:1 to one of two doses of bezuclastinib or placebo. Patients completing Part 1 may continue to Part 3, an open-label extension.

Results: Summit Part 1a enrolled 20 patients; the majority were female (75%) and had an ECOG of 0-1 (90%). Patients utilized a median (range) of 3 (2-7) BSC medications at baseline. Serum tryptase was ≥20 ng/mL in 85% of patients (median: 74 [10 to 592] ng/mL) and 75% were KIT D816V positive with median variant allele frequency 0.5% [0 to 32%]. Median baseline Mastocytosis Activity Score of 43 (22-79) indicated severe disease in most patients. Mean Mastocytosis Quality of Life score at baseline was 56+/- 19, a score which indicates moderate HRQoL impact. 100% of patients completing Part 1a as of the datacut have continued in Part 3.

Conclusions: Summit Part 1 includes ~50 patients with moderate to severe NonAdvSM. Available safety, clinical activity, and patient reported outcome data will be presented.

Funding: Cogent Biosciences, Inc.

F28

Burden of the Untreated Attacks and its Impact on Social, Mental and Physical Health

Cristine Radojicic MD, Paula Busse MD, Maeve O'Connor MD, Julie Ulloa, Sherry Danese, Vibha Desai PhD, Tomas Andriotti MD, Paul Audhya MD, Sandra Christiansen MD

Introduction: HAE Management Guidelines recommend all attacks be considered for treatment to prevent progression and optimize outcomes. Despite availability of on-demand therapies, patients do not universally treat attacks. We examined the burden of untreated attacks and its impact on social, mental, and physical health.

Methods: Individuals with HAE-C1-INH (target n=20) recruited by the US HAE Association completed a 20-minute self-reported online survey. Participants >18yrs old whose last attack (≤3 months prior) was not treated with on-demand treatment, were eligible. The impact of the last attack was assessed using a modified Hereditary Angioedema Quality of Life Questionnaire.

Results: Twenty respondents (80% Type 1 HAE-C1-INH; mean age 39yrs; 75% female; 11 [55%] non-androgen long-term prophylaxis [LTP] users; 9 [45%] on-demand treatment only [OD] users) reported having an average of 10 attacks over the past year, of which only 21% were treated. Fourteen respondents (70%) described their last untreated attack as mild at onset and of these, 7 (50%) progressed to moderate/severe. Five attacks (25%) spread to other locations, including 1 to the larynx and 1 to the face. Fourteen (70%) patients indicated that their last untreated attack had an impact on their energy levels (medium/severe impact indicated by 36% OD [3/9] and 36% LTP [4/11] patients). Twenty-two percent OD (2/9) and 36% LTP (4/11) patients felt socially isolated, 22% OD (2/9) and 55% LTP (6/11) felt reluctant to go out in public, and 5 respondents (25%) felt like a burden to others because they needed help during their last untreated attack.

Conclusions: Patients (including those taking LTP) reported that untreated attacks often progressed in severity, migrated to other locations, and were associated with social isolation and impact on physical/mental health. Results emphasize the need for greater education on the implications of not treating HAE attacks and support guidelines that all attacks should be considered for treatment.

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F29

Amlitelimab Improves Extent and Severity of Disease in Adults with Moderate-to-Severe Atopic Dermatitis (AD): 24-Week Results from a Phase 2b Trial (STREAM-AD)

Stephan Weidinger, MD, PhD; Carolina Guerreiro, PharmD; Andrew Blauvelt, MD, MBA; Ken Igawa, MD, PhD; Christine Weber, MD; Efstathios Zikos, PhD; Jennifer Wang, MA-Statistics; Cori Gray, MS-HOPE.

Introduction: Amlitelimab (SAR445229; KY1005) is a fully human, non-depleting monoclonal antibody that binds OX40 ligand on antigen-presenting cells, potentially inhibiting a key driver of AD pathophysiology. Amlitelimab has previously demonstrated 24-week primary endpoint efficacy in adults with moderate-to-severe AD.

Methods: STREAM-AD (NCT05131477) is a 52-week, randomized, double-blinded, placebo-controlled, Phase 2b trial conducted in 2 parts (24-week Part 1 completed and presented here; 36-week Part 2 ongoing). Adults (18 to <75 years) with moderate-to-severe AD were randomized 1:1:1:1:1 to receive amlitelimab (250 mg + 500 mg loading dose [LD], n=77; 250 mg [no LD], n=78; 125 mg, n=77; 62.5 mg, n=79) or placebo (n=79) every 4 weeks. Here, 24-week secondary outcomes of AD extent and severity are presented, including effects on the SCORing of AD (SCORAD) Index and percentage body surface area (BSA) affected by AD.

Results: Improvements in mean change from baseline at Week 24 were seen across all amlitelimab arms for SCORAD total score and BSA percentage. SCORAD (standard deviation [SD]): amlitelimab 250 mg + LD, −36.19 (24.60); 250 mg (no LD), −27.28 (22.94); 125 mg, −29.96 (25.74); 62.5 mg, -28.48 (21.79); placebo, −15.08 (22.74). Percentage affected BSA (SD): amlitelimab 250 mg + LD, −31.35 (22.43); 250 mg (no LD), −21.82 (21.88); 125 mg, −22.66 (27.32); 62.5 mg, −25.77 (22.09); placebo, −10.45 (20.84).

Conclusion: Amlitelimab improved metrics of disease extent and severity in adults with moderate-to-severe AD in the first 24 weeks of this Phase 2b trial, with greatest improvement seen in the 250 mg + LD arm.

Funding: Sanofi

F30

Improvements on Patient-Reported Outcome (PRO) Measures With 24 Weeks of Amlitelimab Treatment in Adults With Moderate-to-Severe Atopic Dermatitis: Results From a Phase 2b Trial (STREAM-AD)

Andrew Blauvelt, MD, MBA; Harshal Shah, PharmD; Ken Igawa, MD, PhD; Efstathios Zikos, PhD; Christine Weber, MD; Jennifer Wang, MA-Statistics; Cori Gray, MS-HOPE; Stephan Weidinger, MD, PhD

Introduction: Atopic dermatitis (AD) significantly impairs quality of life (QoL), with negative impact correlating with disease severity. Here, we report PRO data from the STREAM-AD trial of adults with moderate-to-severe AD treated with amlitelimab (SAR445229; KY1005), an anti-OX40 ligand monoclonal antibody, vs. placebo.

Methods: STREAM-AD (NCT05131477) is a 52-week, randomized, double-blinded, placebo-controlled, dose-ranging Phase 2b trial in 2 parts (24-week Part 1 completed and presented here; Part 2 ongoing). Adults (18 to <75 years) with moderate-to-severe AD were randomized 1:1:1:1:1 to receive amlitelimab (250 mg with 500 mg loading dose [LD], n=77; 250 mg [no LD], n=78; 125 mg, n=77; 62.5 mg, n=79) or placebo (n=79) every 4 weeks. Patient disease severity/control and QoL were measured by Patient Oriented Eczema Measure (POEM), Dermatology QoL Index (DLQI), and AD Control Tool (ADCT).

Results: Improvements in mean change from baseline at Week 24 were seen across all amlitelimab arms. POEM (standard deviation [SD]): amlitelimab 250 mg with LD, −9.96 (7.89); 250 mg (no LD), −7.21 (8.21); 125 mg, −7.86 (8.57); 62.5 mg, −7.64 (7.01); placebo, −2.19 (7.31). DLQI (SD): amlitelimab 250 mg with LD, −8.33 (7.04); 250 mg (no LD), −6.54 (6.38); 125 mg, −6.74 (8.68); 62.5 mg, −7.69 (7.23); placebo, −2.30 (6.41). ADCT (SD): amlitelimab 250 mg with LD, −7.35 (6.70); 250 mg (no LD), −5.80 (6.19); 125 mg, −6.70 (6.57); 62.5 mg, −6.66 (5.87); placebo, −1.90 (5.05).

Conclusion: Amlitelimab improved metrics of disease severity, disease control, and QoL, with the greatest improvement seen in the 250 mg with LD arm.

Funding: Sanofi

F31

Pharmacokinetics and Pharmacodynamics of Epinephrine Following Administration via Sublingual Film, Autoinjector, or Manual Injection

David Golden MD, Jay Lieberman MD, David Bernstein MD, John Oppenheimer MD, Mark L. Freedman MD, Carl Kraus MD, Steve Wargacki PhD

Rationale: AQST-109, a sublingual film containing a novel prodrug of epinephrine (DESF), is under development for the emergency treatment of Type 1 allergic reactions. The final formulation of AQST-109 was compared with epinephrine delivered by two different approved autoinjectors (EpiPen and Auvi-Q) or by manual injection (IM).

Methods: Data integration was performed across clinical studies, in which healthy volunteers meeting the same exclusion/inclusion criteria received either AQST-109 12mg, or 0.3 mg EpiPen, 0.3mg Auvi-Q and 0.3mg IM. Both studies were randomized, open-label crossover trials evaluating pharmacokinetic and pharmacodynamic parameters for at least 240 minutes post-dose.

Results: Delivery of AQST-109 resulted in comparable epinephrine pharmacokinetics to EAIs or IM. Geometric mean epinephrine Cmax was 457 pg/mL for AQST-109 and 628, 646, and 344 pg/mL for EpiPen, Auvi-Q, and IM, respectively. Median Tmax (minutes) for AQST-109 (15) was most similar to EpiPen (10), with Auvi-Q (30) and IM (50) Tmax being higher. Area under the curve for AQST-109 was between the IM and EAI values for all timepoints between 8 and 60 minutes post-dose. AQST-109 induced a similar PD response across all parameters (systolic blood pressure, diastolic blood pressure and pulse) when compared to either EAI and to IM.

Conclusion: The PK and PD of AQST-109 delivered epinephrine within range of the approved epinephrine manual IM and EAI products. These results demonstrate that the sublingual administration of the novel prodrug in AQST-109 shows promise as a viable needle-free alternative for treatment of Type I allergic reactions.

Funding: Aquestive Therapeutics

F32

Epinephrine Administered via Sublingual Film, Manual Injection, or Auto-Injectors in Healthy Adults: Pharmacodynamic Results

Gary Slatko MD, Shawn Berg, Steve Wargacki, PhD David Golden MD, David Bernstein MD, Jay Lieberman MD, Mark L. Freedman MD

Introduction: Patient/caregiver-administered epinephrine is the first-line treatment for anaphylaxis. Both rapid onset and durability of pharmacodynamic effects of epinephrine are needed to stabilize patients from the most severe symptoms of anaphylaxis, so that they have adequate time to seek emergency medical care.

Methods: This randomized, open-label crossover study evaluated the pharmacodynamics (PD) of epinephrine delivered via sublingual film (AQST-109), manual IM injection or as two different approved auto-injectors (EAIs). Measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate (PR) occurred between 2 and 240 minutes after dosing.

Results: Mean maximum effect (Emax) for SBP and DBP were highest for AQST-109, 20.8mmHg and 12.3mmHg respectively. In addition, the median time to Emax (TE_{max}) occurred earliest with AQST-109 at 11 min across all 3 parameters, compared to manual IM and EAIs which ranged from 19 to 39 min. Changes from baseline in SBP and DBP ≥5 mmHg were sustained from 2 to 60 mins post-dose for AQST-109, but was only achieved for SBP and sustained briefly after the other administration methods.

Conclusion: Changes in SBP, DBP, and PR are key indicators of clinical response to epinephrine in patients experiencing anaphylaxis. AQST-109 elicits a rapid, robust increase in SBP, DBP, and PR that persisted for up to 60 min post-dose, providing adequate time to seek emergency medical care. The data suggest sublingual administration of epinephrine may provide enhanced pharmacodynamic benefits to patients experiencing allergic reactions.

Funding: Aquestive Therapeutics

F33

Predicting Abrocitinib Efficacy at Week 12 in Patients With Moderate-to-Severe Atopic Dermatitis Based on Their Week 4 Response: A Post Hoc Analysis of 4 Randomized Studies

April W. Armstrong, MD, MPH, Andrew F. Alexis, MD, MPH, Andrew Blauvelt, MD, MBA, Jonathan I. Silverberg, MD, PhD, MPH, Mark Levenberg, DO, Gary Chan, PharmD, Fan Zhang, PhD, Luke Fostvedt, PhD, Claire Feeney, MD, PhD

Introduction: Abrocitinib may be initiated at 100 mg/day for the treatment of moderate-to-severe atopic dermatitis (AD), however increasing dosage to 200 mg may benefit some patients. At Week 4 of clinical trials, patients receiving abrocitinib 100 mg achieved approximately 50% to 75% of their Week 12 efficacy responses. This post hoc analysis aimed to identify predictors of response to abrocitinib at Week 12 based on Week 4 assessments.

Methods: Data were pooled from patients with moderate-to-severe AD who received abrocitinib 100 mg/day as monotherapy or with concomitant topical therapy in 4 randomized trials. Data from 70% of patients were examined to identify predictors of response (training cohort). Predictors were tested using the remaining 30% of patients (validation cohort). Dependent variables were ≥75% improvement in Eczema Area and Severity Index (EASI-75) and Investigator's Global Assessment score of 0 (clear) or 1 (almost clear) with ≥2-point improvement from baseline (IGA response) at Week 12. Predictor variables included EASI-50 response at Week 4.

Results: Data of 647 patients were analyzed (training cohort, 453; validation cohort, 194). In the training cohort, Week 12 EASI-75 was achieved by 72% of Week 4 EASI-50 responders and 16% of nonresponders; proportions were 48% and 6% for Week 12 IGA response. In the validation cohort, Week 12 EASI-75 was attained by 69% of Week 4 EASI-50 responders and 23% of nonresponders; proportions were 41% and 12% for Week 12 IGA response. EASI-50 response at Week 4 predicted EASI-75 response at Week 12 with sensitivity of 0.90 and specificity of 0.60; for prediction of Week 12 IGA response, values were 0.94 and 0.48.

Conclusions: EASI-50 response at Week 4 may be a useful predictor of Week 12 response. Patients who failed to reach EASI-50 at Week 4 may be candidates for dose increase to 200 mg to optimize response.

Funding: Pfizer Inc.

F34

Effect of Abrocitinib and Dupilumab on Eosinophil Levels in Patients With Moderate-to-Severe Atopic Dermatitis and With or Without Comorbid Asthma or Allergic Rhinitis: A Post Hoc Pooled Analysis of JADE COMPARE and JADE DARE

Bob Geng, MD, Audrey Nosbaum, MD, PhD, Mark Boguniewicz, MD, Irina Lazariciu, MSc, Claire Feeney, MD PhD, Francisco J. Rebollo, MD, Herwig Koppensteiner, PhD

Introduction: Eosinophilia is common in patients with type 2 inflammatory diseases, including atopic dermatitis (AD), asthma, and allergic rhinitis. This post hoc analysis assessed the effects of abrocitinib and dupilumab on eosinophilia in patients with moderate-to-severe AD, with or without comorbid asthma or allergic rhinitis.

Methods: Data were pooled from patients given abrocitinib (200 mg/day) or dupilumab (300 mg/every two weeks) in two phase 3, randomized trials (JADE COMPARE, NCT03720470; JADE DARE, NCT04345367). Data were subdivided by asthma or allergic rhinitis status based on baseline medical history. The proportion of patients with eosinophilia (>500/mm^3 to ≤1500/mm^3) or hypereosinophilia (>1500/mm^3) was assessed through week 16.

Results: Of 1195 pooled patients, 377 (32%) had asthma; 211 (18%) had allergic rhinitis. Incidence of eosinophilia at baseline was higher in patients with comorbidities than in those without (with/without asthma: 30%/21%; with/without allergic rhinitis: 26%/23%). Regardless of comorbidity status, the proportion of patients with eosinophilia decreased from baseline as early as week 2 and remained low through week 16 with abrocitinib (with/without asthma: 30%/22% [baseline], 12%/10% [week 2] and 11%/9% [week 16]; with/without allergic rhinitis: 25%/24%, 8%/11% and 8%/10%) but not with dupilumab (with/without asthma: 29%/20% [baseline] and 37%/19% [week 16]; with/without allergic rhinitis: 26%/22% and 33%/22%). Similar reductions in the proportion of patients with hypereosinophilia were observed from baseline through week 16 with abrocitinib but not with dupilumab, regardless of comorbidity status.

Conclusions: In this pooled JADE COMPARE/DARE analysis, abrocitinib, but not dupilumab, rapidly resolved eosinophilia in patients with moderate-to-severe AD regardless of asthma or allergic rhinitis status.

Funding: Pfizer Inc

F35

Efficacy of albuterol–budesonide asthma rescue inhaler in adults with moderate-to-severe asthma with exercise as a trigger: post-hoc sub-group analysis of MANDALA

Elliot Israel, MD, Bradley E. Chipps, MD, Richard Beasley, DSc, Reynold A. Panettieri Jr, MD, Samuel Bardsley, MSc, Christy Cappelletti, PharmD, Lynn Dunsire, MSc, Ileen Gilbert, MD, Tim Harrison, MD, Frank Trudo, MD, Alberto Papi, MD

Introduction: Albuterol-budesonide 180/160µg inhaler is FDA approved for as-needed treatment or prevention of bronchoconstriction and to reduce exacerbation risk in patients aged ≥18 years with asthma. In MANDALA (NCT03769090), as-needed albuterol-budesonide 180/160µg reduced severe exacerbation risk by 28% versus albuterol in symptomatic patients ≥18 years with moderate-to-severe asthma on a wide variety of inhaled corticosteroid (ICS)-containing maintenance therapies. Exercise is a well-recognized trigger of asthma symptoms/deterioration. Here, we report the efficacy of albuterol-budesonide 180/160µg in adults in MANDALA who reported exercise among their triggers.

Methods: Primary and secondary endpoints from MANDALA were analyzed post-hoc in the subgroup of adults (≥18 years) reporting exercise as a trigger. Data are reported for the comparison of albuterol-budesonide 180/160µg with albuterol 180µg.

Results: One-third of adults reported exercise as a trigger: albuterol-budesonide 334/979 (34%); albuterol 310/980 (32%). Of these, 35.2% randomized to albuterol and 22.8% randomized to albuterol-budesonide had a severe exacerbation during the study. In this subgroup, albuterol-budesonide reduced the risk of a severe exacerbation by 43% (HR 0.57; 95% CI 0.43–0.77; p<0.001) and annualized severe exacerbation rate by 36% (HR 0.64; 95% CI 0.46–0.90; p=0.009) versus albuterol. Mean (SD) annualized total SCS dose was 220 (1120)mg in the albuterol group and 106 (308)mg in the albuterol-budesonide group (52% reduction).

Conclusions: These post-hoc analyses demonstrate albuterol-budesonide rescue offers the opportunity to reduce severe asthma exacerbation risk and resultant SCS exposure in adults with asthma who reported exercise amongst their triggers.

Funding: AstraZeneca

F36

The Use of Beta-Alanine for the Management of Aquagenic Pruritus

Ami Degala MD and Jai Degala

Introduction: Aquagenic Pruritus is a rare condition associated with severe itching upon contact with water regardless of temperature without any dermatological findings. There is intense itching upon contact with water in any form which starts within minutes and can last up to 120 minutes. The itching is intense and can be debilitating even causing psychological effects and aversion to taking baths or showers. There are no associated cutaneous lesions which differs from Aquagenic Urticaria in which there is evidence of hives. There are various therapeutic options; however, most are ineffective. We report an adolescent male with Aquagenic Pruritus who has been effectively managed with the use of Beta-Alanine.

Case Description: An otherwise healthy 16-year old boy complains of itchiness after being in contact with any type or body of water. There is no associated hives or angioedema. Showers of any temperature, swimming in any type of pool or beach, sweat, and even raindrops induce itching. The itching occurs anywhere water contacts the body, but tends to spare palms and soles. No history of underlying conditions. Not on any regular medications. Symptoms started 6 years prior. CBC and Biochem Profile were normal. Water challenge with wet cloth at room temperature elicited itching but no hives. H1 and H2 Antihistamines were tried but offered no relief. Growing number of Aquagenic Pruritus sufferers have found substantial relief with Beta-Alanine. Using 2 grams prior to water exposure helped reduce and prevent symptoms.

Discussion: This case illustrates effective management of Aquagenic Pruritus with the use of the amino acid, Beta-Alanine. This therapy warrants further exploration in medical literature for optimal management and therapeutic options. The effectiveness of Beta-Alanine may also help expose a different mechanism of the itch pathophysiology.

F37

Ferret-Monosensitization: An Unusual Allergen in Pediatric Rhinosinusitis

Travis Satnarine, Gary Kleiner, and Melissa Gans

Introduction: Pediatric allergic rhinitis, involving nasal mucosal inflammation due to specific allergens, is common. Allergy to domestic ferrets (Mustela putorius) is seldom reported, and the associated allergens are poorly understood.

Case Presentation: A 13-year-old male presented with persistent nasal congestion, snoring, and recurrent nosebleeds. Assessment of the Sinonasal Outcomes Test (SNOT-22) gave a score of 20 (range 0 to 100), indicating moderate rhinosinusitis-related health burden, while the Nasal Obstruction Visual Analog Scale (VAS) score was 75 (range 0 to 100), indicating significant nasal obstruction. Evaluation by pediatric otolaryngologist suggested a multifactorial component including septal deviation and hypertrophied inferior turbinates.
Laboratory testing indicated sensitization to ferret epithelium, with all other tested allergens negative, *Table 1*. The patient has a pet ferret who sleeps in his room. Skin prick testing was offered for other aeroallergens, with the family expressing willingness at the next visit if symptoms did not improve. Surgical intervention was considered if recommended by the otolaryngologist. The ongoing plan involves optimized medical therapy, including sinus rinses, intranasal corticosteroids, cetirizine 10 mg daily, and montelukast 10 mg daily. Home aeroallergen control measures were discussed, including using an air purifier with a filter, maintaining low humidity in the bedroom, and employing allergen-resistant bedding, keeping pets out of the bedroom. The patient was scheduled for follow-up monitoring.

Conclusions: The identification of monosensitization to ferrets prompts a broader discussion on the significance of targeted allergen assessment in pediatric allergic rhinitis. This finding sheds light on the potential oversight of specific allergens, such as ferret dander, in routine diagnostic protocols. Sensitized individuals may develop reactions to ferret hair, urine, and feces, and can exacerbate asthma, allergic rhinitis, and cause contact dermatitis.

F38

A Single Center Case Series Study of Immune Dysregulation Presenting as Treatment-Refractory Autoimmune Cytopenia in Kabuki Syndrome

Kranthi Nomula, MD; Merve Nida Gokbak; Priya K. Patel, MD; David E. Potts, MMSc; Jolan E. Walter, MD, PhD

Introduction: Kabuki Syndrome (KS) is a rare genetic disorder characterized by distinctive facial features, skeletal anomalies, and developmental delays. While its impact on various organ systems is well-documented, understanding of immune dysregulation in KS remains limited. Autoimmune cytopenia, including autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP), has been reported in individuals with KS, posing significant diagnostic and therapeutic challenges. This study aimed to investigate clinical presentation, diagnostic approach, and management strategies for immune dysregulation presenting as treatment-refractory autoimmune cytopenia in patients with Kabuki Syndrome.

Objectives: The study aimed to characterize the clinical manifestations, genetic profiles, and treatment responses of patients with Kabuki Syndrome presenting with autoimmune cytopenia. Additionally, it sought to elucidate the challenges and complexities in managing this condition.

Methods: A retrospective case series analysis was conducted involving three patients diagnosed with Kabuki Syndrome and presenting with treatment-refractory autoimmune cytopenia. Clinical data including medical histories, physical examinations, laboratory investigations, genetic testing results, imaging studies, and treatment regimens were reviewed and analyzed.

Results: All three patients exhibited complex medical histories, including recurrent episodes of AIHA and ITP resistant to standard treatments. Despite receiving multiple therapies, including steroids, intravenous immunoglobulin (IVIG), rituximab, mycophenolate, and sirolimus, patients experienced persistent or recurring cytopenia. Adverse effects such as lung toxicity and mucositis were encountered during treatment, necessitating modifications.

Conclusions: The study highlights the challenging management of immune dysregulation in Kabuki Syndrome, particularly autoimmune cytopenia, which often proves refractory to standard therapies. Collaboration between hematologists and immunologists is essential for comprehensive patient care and treatment optimization. The findings underscore the need for further research to elucidate the underlying mechanisms of immune dysregulation in Kabuki Syndrome and explore novel therapeutic avenues to improve patient outcomes. Additionally, the study emphasizes the importance of early diagnosis and multidisciplinary management in addressing the complex medical needs of individuals with Kabuki Syndrome and autoimmune cytopenia.

F39

Severe Atopic Dermatitis and Asthma Pediatric Patient Shows Marked Improvement on Tralokinumab While Refractory on First Line Therapy

N. Navasero, BS, K. Smiley, PA-C, A. Tambay, BS, L. Loop, BS, B. Geng, MD

Introduction: This case report presents a 12-year-old male patient with severe atopic dermatitis (AD) and asthma, who exhibited a positive response to treatment with tralokinumab, a monoclonal antibody targeting interleukin-13. The patient had a long-standing history of poorly controlled AD, with multiple failed attempts at managing symptoms using topical steroids, immunosuppressants, and systemic therapy such as dupilumab and abrocitinib; and whose asthma was also concurrently treated with mepolizumab.

Methods: The patient's clinical course was documented through a comprehensive review of electronic medical records, including multidisciplinary eczema and asthma clinic notes, patient reported outcomes and healthcare utilization data. Key parameters such as the Eczema Area and Severity Index (EASI), Body Surface Area (BSA) involvement, Validated Investigator Global Assessment (vIGA) scores, and medication adherence were closely monitored.

Results: Prior to initiating tralokinumab, the patient's AD was poorly controlled, with an EASI of 13.5, BSA of 22.3%, and vIGA of 4 (severe) as of August 2023. While on dupilumab, eczema did improve; however, therapy was discontinued due to intolerable local injection site reactions. He was then treated with abrocitinib (100 mg and 200 mg dose trials) and had no clinical improvement in his eczema, and experienced persistent flares, sleep disturbances, and impaired quality of life. After initiating tralokinumab in January 2024, the patient demonstrated a remarkable improvement in AD severity. By March 2024, the EASI had decreased to 3.5, BSA to 2.1%, and vIGA to 1 (almost clear). Additionally, the patient reported better sleep quality and reduced itch intensity (pruritus rating of 2). Skin clearance continued to improve through 3.5 months on tralokinumab at the most recent office visit. Asthma control also improved, with fewer weekly exacerbations. Moreover, the patient has not been admitted to the emergency room or treated with systemic steroids for asthma exacerbation since December 2023.

Conclusion: This case report highlights the promising efficacy of tralokinumab in managing moderate-to-severe AD in a pediatric patient who had intolerable side effects or no response to first-line biologic agents and JAK inhibitors. The significant improvement in atopic dermatitis disease severity and quality of life observed with tralokinumab treatment underscores the need for further investigation of this therapeutic option in younger populations with refractory AD

F40

Shared Decision-Making as a Resource for Assessing Disease Burden and Management of Chronic Spontaneous Urticaria

Caitlin Gutierrez, RN, Don Bukstein, MD, Ted Huwe, BA

Introduction: Diagnosis and treatment of Chronic Spontaneous Urticaria (CSU) is founded on evidence-based guidelines. Many give conditional recommendations, however specific patient burdens, needs, and benefits of therapy have not been outlined in these guidelines. The aim of this Shared Decision-Making (SDM) tool was to characterize the specific needs and treatment goals of patients with CSU from the patient's perspective.

Methods: The SDM tool on CSU was validated by SDM Central's network of subject matter experts including experts from the Global Allergy and Airways Patient Platform (GAAPP). Experts reviewed the tool for accuracy, appropriateness of questions, and provided suggestions. The tool was published on the GAAPP website and invitations to participate were distributed to the GAAPP's patient membership list. Responses from surveys were stored and analyzed using Airtable.

Results: Data from 172 surveys were analyzed. Responses on patient difficulty with sleep, exercise and social engagement were examined to determine the burden of CSU (Figure 1). Responses across categories were diverse among patients with CSU. Patient preferences for treatment options were similarly varied (Figure 2) with 49% of respondents reporting that they would like a follow up from their provider to discuss their options.

Conclusions: Population-level information about the burden and management of CSU can be gleaned from data captured in SDM tools. Innovative drugs and treatments may increase overall outcomes, however these data show that CSU management needs to be individualized since disease burden and treatment preferences vary widely between patients. Regardless of the treatment chosen, Shared Decision-Making in the management of CSU should be a standard of practice.

F41

An Atypical Hypersensitivity Reaction to Acetaminophen

Danielle Harrison, MD, Cheryl Rozario, MD

Introduction: Acetaminophen is a common analgesic and antipyretic medication used for treatment of fever and pain that can lead to urticaria or even anaphylaxis in rare cases.

Case Description: A 51-year-old male presented with an episode of anaphylaxis, specifically urticaria and hypotension, and recurrent episodes of diffuse urticaria within 30 to 45 minutes of acetaminophen use. The initial episode of anaphylaxis occurred 30 minutes after ingesting 1000 mg of acetaminophen and within 3 hours of eating leftover charcuterie meats from a recent camping trip and taking his 4th dose of doxycycline for empiric treatment of Lyme disease (later serologies found negative). He was evaluated in the ED and treated with IV solumedrol, diphenhydramine, and famotidine with resolution of his symptoms. He had two subsequent episodes of suspected urticarial rash in the setting of acetaminophen at lower dosages within 30 to 45 minutes of use and in the absence of doxycycline and mammalian meat. These episodes were suspicious for an IgE-mediated hypersensitivity to acetaminophen or as a result of COX-1 inhibition, especially given high dose usage with initial reaction. Medical history was negative for chronic spontaneous urticaria, other NSAID use, pruritus, eczema, or asthma. Alpha gal IgE and baseline tryptase were reassuring. An in office oral food challenge to ground beef and celecoxib were negative. He continues to avoid doxycycline, acetaminophen, and all selective COX-1 inhibitors without any further episodes of urticaria or anaphylaxis.

Discussion: Acetaminophen at high doses [ie. 1000 mg or higher], can lead to COX -1
inhibition, leading to shunting of arachidonic acid metabolism towards the 5-lipoxygenase pathway, which results in increased synthesis and release of cysteinyl leukotrienes inflammatory mediators and worsening urticaria. Immediate hypersensitivity to acetaminophen may be IgE-mediated or potentially related to COX-1 inhibition.