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Efficacy and safety of amlitelimab (an OX40 ligand antibody) in patients with moderate-to-severe atopic dermatitis: 52-week results from a Phase 2b trial (STREAM-AD)

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Introduction: Amlitelimab is an OX40 ligand (OX40L) monoclonal antibody inhibiting OX40L-OX40 interactions. Data from the 28-week amlitelimab maintenance/withdrawal period (Part 2) of the Phase 2b (STREAM-AD, NCT05131477) dose-ranging trial in adults with moderate-to-severe atopic dermatitis (AD) are presented.

Methods: STREAM-AD Part 2 included clinical responders from Part 1, defined as participants achieving EASI-75 and/or IGA 0/1 at Week 24. Of 390 participants enrolled in Part 1, 190 entered Part 2. Participants were re-randomized 3:1 to withdraw treatment or continue pre-Week 24 subcutaneous Q4W dose (250mg with 500mg loading dose (LD), n=34 [treatment withdrawal]/n=13 [continuing]; 250mg, n=28/n=12; 125mg, n=33/n=12; 62.5mg, n=35/n=7; placebo responders continuing placebo, n=16), and were followed to Week 52 for efficacy. Statistical analysis was conducted using two approaches: imputing endpoint as non-responder after rescue medication use (NRI) or including all measurements regardless of rescue use (treatment policy).

Results: Maintenance of EASI-75 and/or IGA 0/1 response at Week 52 was observed in 59%, 63%, 55%, and 66% of clinical responders withdrawn from Q4W dose of 250mg with LD, 250mg, 125mg, and 62.5mg, respectively (NRI). Using treatment policy, 77%, 82%, 67%, and 74% maintained response off-drug, respectively. Those continuing treatment had numerically higher maintenance response rates. AD-related biomarkers remained decreased over 28 weeks, including in participants withdrawn from amlitelimab with ≥95% of the drug eliminated from serum for the last 8 weeks. The safety profile remained generally consistent with Part 1 without new concerns identified in Part 2.

Conclusion: Maintenance of clinical responses were demonstrated for 28 weeks in the majority of patients, both on- and off-amlitelimab.

Funding: Kymab LTD, a Sanofi company.

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

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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.

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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

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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.

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

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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

Real-world Impact of Treated **Hereditary Angioedema Attacks on Patients' Employment and Work Productivity**

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

Introduction: Hereditary angioedema (HAE) is a rare genetic disease associated with unpredictable attacks of tissue swelling. We examined the impact of the patients' last treated attack on their ability to work and whether this was diminished among those having attacks while receiving long-term prophylaxis (LTP).

Methods: Patients with type I/II HAE completed an online survey. Participants ≥12yrs old treated ≥1 HAE attack with an on-demand (OD) therapy in the prior 3 months. The Work Productivity and Activity Impairment Questionnaire: General Health assessed the impact of the last treated attack on participants' ability to work during 7 days following attack onset.

Results: Respondents included 80 adults and 14 adolescents, of which 42 patients self-reported as employed at the time of their last treated attack. Of those, 24 (57%) managed HAE with OD only, while 18 (43%) were receiving LTP. Sixty-seven (72%) rated their attack severity as moderate to very severe (72% OD; 71% LTP). Median (interquartile range) time from attack recognition to OD treatment was 2hrs (1-4hrs). Twenty (48%) patients were moderately to completely unable to do their job due to their last attack (46% OD; 50% LTP). Average impairment for overall ability to work was 39% (36% OD; 43% LTP), and the average absenteeism was 15% (13% OD; 17% LTP). Forty patients worked ≥1hr in the 7 days following the attack. Of those, 14 patients (35%) indicated that their last treated attack modestly to severely impacted their productivity (35% OD; 41% LTP); mean impairment (presenteeism) at work was 35% (33% OD; 37% LTP).

Conclusions: Despite treatment with OD therapy, HAE attacks impacted the work lives of employed patients resulting in impairments in their ability to work, substantial absenteeism, reduced productivity, and presenteeism among those who were able to work. The impact was similar among those managed with OD treatment only and those receiving LTP.

Funding: KalVista Pharmaceuticals

Real-World Impact of Treated **Hereditary Angioedema Attacks on Patients' Quality of Life**

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Introduction: Hereditary angioedema (HAE) is a rare genetic disease associated with unpredictable attacks of tissue swelling. We examined the impact of the patients' last treated HAE attack on physical and social components of quality of life (QoL) and the effect of early treatment.

Methods: Patients with type I/II HAE completed an online survey. Participants were ≥12 years old and treated ≥1 HAE attack with an on-demand therapy in the past 3 months. Physical and social QoL was assessed using modified Hereditary Angioedema Quality of Life Questionnaire.

Results: Respondents included 80 adults and 14 adolescents; 54% taking long-term prophylaxis (LTP) and 46% using on-demand therapy only (OD). Fifty-five percent rated their attack severity as moderate and 16% as severe or very severe. Median (interquartile range) time from attack onset to on-demand treatment was 2 hours (1-5 hours), with 19% treating in <1 hour. Sixty-five (69%) patients (68% OD; 71% LTP) indicated that their last attack had a medium/severe impact on their energy level and 32 patients (34%) indicated their last attack prevented participation in social activities (35% OD; 35% LTP). Of the patients who treated their attack in <1 vs ≥5 hours, 56% and 70%, respectively, indicated their attack had a medium/severe impact on their energy level, and 22% and 42% reported it prevented participation in social activities. Isolation due to HAE attack was experienced by 35 (37%) patients (33% OD; 41% LTP; 28% if treated <1 hour). Thirty-seven (39%) of patients (44% OD; 35% LTP) felt like a burden to people around them because they needed help treating their attack.

Conclusions: These results indicated patients' physical and social QoL was affected by their HAE attack, regardless of being on LTP. Attacks treated in <1 hour were associated with a lower impact on QoL, suggesting that education focused upon early attack treatment may be beneficial.

Funding: KalVista Pharmaceuticals

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

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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

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

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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

Insights Into APDS: Revealing the Patient Experience

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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

Dupilumab Induces Clinical Remission in Children With Uncontrolled, Moderate-to-Severe, Type 2 Inflammatory Asthma

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Introduction: Sustained absence of exacerbations, normal lung function, controlled symptoms, and no systemic corticosteroid use in a 12-month period have been proposed as a composite multicomponent endpoint for on-treatment clinical remission in adults with asthma. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukins 4/13, central drivers of type 2 inflammation. In the phase 3 LIBERTY ASTHMA VOYAGE study (NCT02948959), dupilumab reduced annualized severe exacerbation rate and improved lung function and asthma control vs placebo in children aged 6 to 11 years with moderate-to-severe asthma and type 2 inflammation (baseline blood eosinophil count ≥150 cells/μL or fractional exhaled nitric oxide ≥20 ppb). Safety was consistent with the known dupilumab safety profile, with the addition of helminth infections. This post hoc analysis assessed the effect of dupilumab in achieving on-treatment clinical remission in children using a proposed composite, multicomponent endpoint.

Methods: We evaluated the proportions of patients in VOYAGE meeting the composite endpoint for on-treatment clinical remission during 52 weeks on treatment using criteria: no exacerbations/use of oral corticosteroids; above the lower limit of normal for pre-bronchodilator ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (z-score >−1.64) and pre-bronchodilator FEV_1 (z-score >−1.64); and 5-item Asthma Control Questionnaire (ACQ-5) score <0.75/ <1.5.

Results: The analysis included 350 children (placebo, n=114; dupilumab, n=236). At baseline, no children in either treatment group met the requirements for remission using ACQ-5 <0.75. At Week 52 a significantly greater proportion of children treated with dupilumab vs placebo achieved clinical remission (41.9% vs 23.7%; *P*=0.0008). Similar results were seen using ACQ-5 <1.5.

Conclusion: Dupilumab vs placebo significantly increased the percentage of patients with uncontrolled, moderate-to-severe asthma and type 2 inflammation who met the proposed on-treatment clinical asthma remission composite endpoint by Week 52 of VOYAGE.

Funding: Sanofi and Regeneron Pharmaceuticals, Inc.

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

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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.

Funding: KalVista Pharmaceuticals

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)

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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

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)

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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

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

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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

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

Relief and Resolution of Attack Symptoms Following On-Demand Treatment With a Single Dose of Oral Bradykinin B2 Receptor Antagonist Deucrictibant Immediate-Release Capsule in Patients With Hereditary Angioedema

H. Henry Li, MD, PhD; John Anderson, MD; Marc A. Riedl, MD, MS; Peng Lu, MD, PhD; Marcus Maurer, MD

Introduction: Hereditary angioedema (HAE) attacks are caused by excess bradykinin activating bradykinin B2 receptors. Deucrictibant is a potent, orally administered antagonist of the bradykinin B2 receptor under development for on-demand and prophylactic treatment of HAE attacks.

Methods: RAPIDe-1 (NCT04618211) was a Phase 2, double-blind, placebo-controlled, crossover trial of deucrictibant immediate-release (IR) capsule for treatment of HAE-1/2 attacks. Seventy-four participants were enrolled (Canada, Europe, Israel, UK, US). Substantial symptom relief was assessed by time to ≥50% reduction in the 3-symptom composite visual analogue scale (VAS-3). Symptom resolution was assessed by time to "almost complete or complete symptom relief" using VAS-3 (all 3 individual VAS scores ≤10) as well as achievement of "a lot better or resolved" on Treatment Outcome Score patient-reported outcome (TOS PRO).

Results: Attacks treated with a single dose of deucrictibant IR capsule at doses of 10, 20 or 30 mg achieved earlier substantial symptom relief (median time: 3.3-4.0 hours) and symptom resolution (5.8-20.0 hours) by VAS-3 compared with attacks treated with placebo (22.8 and 42.0 hours, respectively). The percentage of attacks achieving symptom resolution by VAS-3 within 24 hours was approximately 5-fold greater with deucrictibant IR capsule (71.4-78.4%) compared with placebo (15.7%). Symptom resolution by TOS PRO was also achieved earlier for attacks treated with a single dose of deucrictibant IR capsule, with a median time of 4.0-5.9 hours vs. 23.3 hours for placebo-treated attacks. The percentage of attacks achieving symptom resolution by TOS PRO within 24 hours for deucrictibant IR capsule was 78.6%-86.2% compared with 22.4% for attacks treated with placebo.

Conclusions: Primary and post-hoc analyses of the RAPIDe-1 Phase 2 trial provide consistent evidence that the majority of HAE attacks achieved symptom resolution within 24 hours after a single dose of oral deucrictibant IR capsule.

Funding: RAPIDe-1 is a Pharvaris

Phase 2 OLE Two-Year Analysis of Donidalorsen Taken Every 4 Weeks or Every 8 Weeks in Patients with Hereditary Angioedema

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Introduction: Hereditary angioedema (HAE) is a rare disease characterized by unpredictable, recurrent bouts of swelling that may be severe or fatal. Donidalorsen is an investigational antisense oligonucleotide designed to reduce plasma prekallikrein production via degradation of prekallikrein mRNA. We report results from the 2-year open-label extension (OLE) (ISIS 721744-CS3, NCT04307381) of a phase 2 randomized study with donidalorsen in patients with type I or type II HAE.

Methods: This interim analysis included fixed (weeks 1–13; donidalorsen 80 mg subcutaneously every 4 weeks [Q4W]) and flexible (weeks 17–105; donidalorsen 80 mg Q4W, 80 mg every 8 weeks [Q8W], or 100 mg Q4W) treatment periods. Patients could switch to 80 mg Q8W if they were HAE attack-free for ≥12 weeks after entering the OLE. Mean monthly attack rate and changes in quality of life were compared with baseline of the phase 2 randomized study (ISIS 721744-CS2, NCT04030598).

Results: Of 17 patients, 14 completed 2 years of treatment. Study drug-related treatment-emergent adverse events reported in >1 patient were injection site reaction and discoloration (n=2, 11.8%, each). Among all patients, HAE attack rate decreased by mean 96% (95% CI: −99.5 to −92.6; median: 99.1%) to mean 0.06 attacks per month (95% CI: 0.02–0.10; median: 0.04) from baseline. Eight patients switched to 80 mg Q8W dosing, of whom 5 remained attack-free after 2 years. Mean monthly HAE attack rate decreased by mean 83% (95% CI: −113.8 to −52.0; median: 100.0%) to mean 0.29 attacks per month (95% CI: −0.21 to 0.79; median: 0.00) from baseline in patients who switched to Q8W dosing. Mean total angioedema quality-of-life score improved in all patients by 27 points.

Conclusions: Data from the 2-year OLE demonstrated that donidalorsen was well tolerated and effectively reduced HAE attack rate in a sustained fashion. These results warrant further clinical investigation.

Funding: Ionis Pharmaceuticals.

C1 Esterase Inhibitor (C1-INH) Response as a Supportive Diagnostic Criterion for Patients With Suspected Hereditary Angioedema With Normal C1-INH

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Introduction: Hereditary angioedema (HAE) with normal C1-INH level (HAE-nl-C1INH) diagnostic criteria include recurrent angioedema history; normal/near-normal levels of C4, C1-INH, and C1-INH function; and either an associated genetic variant or family history of recurrent angioedema plus lack of response with high-dose antihistamines. A rapid, durable response to a bradykinin-targeted medication is considered supportive.

Methods: A retrospective medical records review (6 centers) was conducted for angioedema or HAE codes to evaluate the diagnostic process for HAE-nl-C1INH in clinical practice.

Results: Thirty-one patients with HAE-nl-C1INH were identified, with the majority female (87.1%) and a mean age of 46.2 years (range, 16-74 years). All patients had experienced recurrent angioedema, with documentation of the ineffectiveness of antihistamine and/or mast cell–targeted therapies. Laboratory data (not during angioedema attacks) supported normal/near-normal levels of C4, C1-INH, and C1-INH function. Genetic testing was reported for 8 patients, with no known pathogenic genetic variants of HAE identified; 1 patient had a plasminogen gene mutation (associated with HAE-nl-C1INH). Diagnosis of HAE-nl-C1INH was confirmed in the 31 patients via a favorable response (symptom reduction/resolution within a few hours) after single-dose administration of intravenous rhC1-INH (weight-based dosing; maximum, 4200 U) during an angioedema attack. Subsequent inclusion of prophylaxis and/or on-demand treatment (eg, rhC1-INH) has reduced angioedema attack frequency/severity. Only 9 of 30 (30.0%) patients with documented information had been aware of a family history of recurrent angioedema/HAE. For 3 patients (10%), several family members were subsequently diagnosed/thought to have HAE-nl-C1INH after patient's diagnosis was established.

Conclusions: A family history of recurrent angioedema may not be apparent, and reliance on family history as a diagnostic criterion may delay accurate diagnosis and patient access to effective treatment. This case series supports that responsiveness to C1-INH replacement therapy (eg, rhC1-INH) may also be a useful supportive diagnostic criterion for HAE-nl-C1INH.

Funding: Pharming Healthcare, Inc.

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.

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.

Association Between Nickel and Propolis on Patch Testing

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Introduction: Patch testing is a diagnostic tool that assesses which allergen a person reacts to through controlled exposure and monitored reaction. Nickel is one of the most common allergens with approximately18.5% of patch tests positive for nickel. However, it is known to cross react with other allergens, which can interfere with diagnosis and treatment. For example, propolis, an allergen derived from beeswax, has reported cases of nickel contamination. This study aims to determine if those who react to nickel are also more likely to also react to propolis on patch testing due to the potential contamination.

Methods: A retrospective chart review was conducted with the following inclusion criteria: a dermatology patient, 18+ years of age, insurance codes CPT 95044 or Z01.82 for patch testing, and the encounter fell from December 1, 2000 to September 1, 2023. Patients were excluded if they did not meet the above inclusion criteria, if the patch test was placed or read incorrectly, or if nickel and propolis were not both tested. If there were multiple episodes of patch testing during this period, only the first instance was included.

Results: A total of 135 out of 170 cases were analyzed. Of the 135 analyzed, the average age was 51 with 68.1% female. A Chi Squared Analysis with a significance level of a= 0.05 was conducted and resulted in $X^2 = 0.812$, p-value = 0.3675.

Conclusions: While our data was not significant, we believe this might be secondary to a type II error. Our sample size of positive reactions was relatively small, with only 17 positive nickel and 9 positive propolis reactions total. Therefore, we plan to conduct a prospective study with concomitant propolis testing on metal-only patch tests to obtain a more robust sample size.

Retrospective Review of Sesame Oral Food Challenges at the University of Miami over the Past 10 Years

Valishti Pundit MD; Jennifer Gebbia APRN; Gary Kleiner, MD PhD; Melissa Gans, MD

Introduction: Sesame became the 9th top food allergen in the US in January 2021. As of January 2023, US food and supplements require sesame labeling. This study adds insights into sesame allergy demographics.

Methods: Following local Institutional Review Board approval, a retrospective analysis was undertaken. Data from electronic medical records of individuals aged 0-22 who underwent nonblinded oral food challenges (OFCs) at the University of Miami from January 2013 to December 2023 were extracted. Among 297 total food challenges identified, sesame challenges comprised only 3% (n=9).

Results: The 9 challenges represented 7 total patients as 2 patients had repeat challenges. Patient #2 underwent 2 separate challenges 1 year apart and failed both times. Patient #3 underwent a first challenge during which he tolerated 20 sesame seeds and then a second challenge during which he failed to “a pea size of tahini.” 8/9 challenges were with tahini, with a successful challenge requiring a cumulative dose of 1-2 tablespoons of tahini. The mean age of the participants was 32 months. Only one patient (1/7, 14%) identified as Hispanic White; all others identified as non-Hispanic White (6/7, 86%). 5 of 9 (56%) failed, with an equal sex distribution. The majority failed at a cumulative dose of ≤0.5 teaspoon tahini, except for one patient who failed at 2 teaspoons. No significant correlation was found between skin prick tests and total specific serum IgE levels with OFC outcomes. Of the four patients who had Ses i 1 component testing, those with specific IgE levels >1.23 IU/mL failed, and there was a correlation between how high the level was and the severity of reaction as Patient #3 with the highest level at 2.66 IU/mL required epinephrine and emergency room management. Those with Ses i1 < 0.38 IU/mL passed. There was no correlation between Ses i1 and the ability to tolerate sesame seeds as Patient #3 passed the 20-seed challenge. Among failed patients, 2/5 (40%) required in-office epinephrine administration, while 1/5 (20%) required emergency room treatment.

Conclusions: Families should be advised on the heightened allergic potency of tahini due to the absence of the protective sesame shell, compared to sesame seeds. Follow-up of sesame-allergic patients is crucial to determine potential resolution over time. Ses i1 testing may offer better predictability for oral graded challenge outcomes and reaction severity, necessitating further investigation. Allergists conducting such challenges must be ready for severe reactions, requiring prompt intervention and potential transfer to emergency care.

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

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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

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.

Early Clinical Improvement of Anosmia and Sinus Nitric Oxide in CRSwNP Subjects treated with Dupilumab

Miguel J Lanz MD, Lianet Herrera Cespedes NP, Claudia P Eisenlohr MIB

RATIONALE: Patients with Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) have a high morbidity of anosmia, yet there are few noninvasive biomarkers to measure treatment response. Nitric oxide is found in paranasal sinuses at 100x higher levels than the lungs and is vital for its antimicrobial/mucociliary activities and vasodilatory properties. Dupilumab has been shown to improve anosmia in two weeks by UPSIT, SNOT-22, and Loss of Smell (LoS) scoring.

METHODS: Adults with CRSwNP confirmed by CT or endoscopy were consented to receive Dupilumab 300mg, Q2 weeks, for 18 weeks. Subjects with polyposis despite treatment with steroids and/or history of sinus surgery were recruited. Measurements of sinus NO (sNO) from the nostril while humming, nasal NO (nNO) while breath holding, and FeNO while exhaling were collected at baseline and Q1,-2,-4,-8,-12,-16,-18 weeks. Olfactory impairment was measured by UPSIT, SNOT, and LoS at every visit.

RESULTS: Sixteen adults, 12 females, were enrolled having a mean age 43 years (23-53). Baseline mean sNO of 434ppb (203-665) significantly increased at Q2 weeks to 1150ppb (684-1616), *(*$p<0.05$*)*. Significant improvements in scoring at baseline to Q2 weeks for UPSIT 28 to 31, SNOT 54 to 33, and LoS 2.3 to 1.5, and weak correlations of sNO with UPSIT (0.48) and SNOT (-0.49) were found. No significant changes in FeNO or nNO were found. Mean baseline blood eosinophil was 306 cells/uL and total IgE was 148 IU/mL. Baseline allergen sensitivity by skin testing and labs were found in 9 subjects, and 14 subjects had low pneumococcal antibody titers.

CONCLUSIONS: Our novel data reveals Sinus NO improvement with treatment response in anosmia as early as two weeks after the initial Dupilumab administration, similarly as other anosmia measures. This improvement in Sinus NO with anosmia improvement in CRSwNP is unique in the literature.

Eosinophilic myopericarditis secondary to ANCA-negative eosinophilic granulomatosis with polyangiitis (EGPA)

Christian Gomez Hernandez, MD; Erika Tsutsui, MD; Sneha Bupathi, MD; Mary-Lee Wong, MD

Introduction: Eosinophilic granulomatosis with polyangiitis (EGPA) is a form of anti-neutrophil cytoplasmic antibody (ANCA)-associated small-vessel multisystem vasculitis characterized by asthma, eosinophilia, chronic rhinosinusitis and pulmonary involvement. This report highlights a case of eosinophilic myopericarditis, a rare complication of EGPA.

Case Report: A 46-year-old woman with a medical history of ulcerative colitis and adult-onset asthma presented to the ED with chest pain and intermittent palpitations for one week. Of note, she was undergoing outpatient evaluation for EGPA due to adult-onset asthma, vocal cord polyps, chronic urticaria, mononeuritis multiplex and peripheral eosinophilia. On examination, she had no murmurs or abnormal heart sounds, and her legs were well perfused with no pitting edema. Laboratory studies were significant for an elevated troponin of 602 ng/L, leukocytosis of 26 K/ul with an eosinophil absolute count (EAC) of 14.5 K/uL and elevated inflammatory markers including an ESR of 98 mm/hr and a CRP of 35 mg/L. Further workup revealed an ANA with a 1:40 cytoplasmic pattern, elevated IgE of 383 IU/m and negative tryptase, c/p-ANCA, and anti-MPO/PR3 antibodies. EKG did not demonstrate ischemic changes. Imaging included a TTE with new HF with a reduced EF of 40% and a mild pericardial effusion, and chest tomography showed bilateral ground-glass opacities. LHC showed normal coronaries and RV endomyocardial biopsy demonstrated eosinophilic myocarditis with no evidence of necrosis. She received a course of high-dose methylprednisolone and cyclophosphamide with normalization of laboratory abnormalities and symptomatic resolution. She was discharged home on a steroid taper, GDMT therapy and close follow up.

Discussion: This patient had eosinophilic myopericarditis, a rare and fulminant condition associated with EGPA, HES, and hypersensitivity myocarditis. In this patient's clinical setting, it is most likely a complication of underlying EGPA. Prompt diagnosis with endomyocardial biopsy and treatment with immunosuppressive therapy is necessary to prevent rapid deterioration.

Addressing Health Inequities: Understanding the Impact of Socioeconomic Factors on Acute Life-Threatening Asthma Exacerbations

Christian Gomez Hernandez, MD; Wenchy Tan, MD; Sneha Bupathi, DO; Mary Lee-Wong, MD

Introduction: Asthma, a chronic respiratory ailment that impacts approximately 25 million individuals in the U.S. annually, is known to have varying prevalence across income brackets. This study aims to determine the extent to which such disparities contribute to in-hospital outcomes in patients admitted for acute asthma exacerbations.

Methods: This was a retrospective cohort study which utilized data from the national inpatient sample database to identify patients who were admitted for an acute asthma exacerbation between January 2017 and December 2019. Primary endpoint was requiring mechanical ventilation. Secondary outcomes included all-cause in-hospital mortality and length of stay (LOS). Weighted multivariable logistic regression and chi-square were used to analyze outcomes while controlling for Elixhauser- comorbidities, age, gender, and race/ethnicity.

Results: Sample included 58,312 patients admitted for an acute asthma exacerbation. Baseline characteristics revealed a mean age of 54 with 38,091 females. Compared to the lowest income quartile, the highest income quartile individuals are at lower odds of mechanical ventilation (OR: 0.76, 95% CI 0.56-0.99). When assessing insurance plans, Medicaid patients showed higher odds of mechanical ventilation than those with Medicare (OR 1.75, 95% CI 1.30-2.37). In terms of LOS, patients in the highest income quartile had shorter LOS compared to those in the lowest quartile ($p<0.001$), and similar trends were observed for Medicare patients relative to Medicaid recipients ($p=0.020$). There was no significant difference in all-cause mortality when accounting for income and insurance plan.

Conclusions: Social determinant of health variables affect inpatient outcomes of asthma hospitalizations. Our studied demonstrated that patients with lower income and Medicare insurance plans had higher rates of mechanical ventilation need and LOS, as compared to those in the highest income groups and Medicaid plans, respectively. Although no significant impact to all-cause mortality, further research is needed.

Dapsone-Induced Methemoglobinemia in Patient with Urticarial Vasculitis and Normal G6PD: A Case Report

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Introduction: Urticarial vasculitis (UV) is a rare, mostly idiopathic, autoimmune disease that can signify a therapeutic challenge due to variable treatment response. We present a case of UV refractory to standard therapy and Omalizumab, which responded to Cyclosporine and Dapsone; however developed methemoglobinemia, an unexpected complication of Dapsone in the setting of normal levels of glucose-6-phosphate dehydrogenase (G6PD).

Case Presentation: A 45-year-old woman with history of allergic rhinitis and asthma presented with one month of persistent generalized urticaria, recurring sporadically since age 15. Despite treatment with prednisone, doxepin, cetirizine, famotidine, hydroxyzine, and Montelukast, symptoms persisted. Omalizumab was initiated, and a few weeks later she developed diffuse tingling, burning sensation of skin, worsening pruritus, painful hives, and bruising after significant sunlight exposure. A skin punch biopsy confirmed the diagnosis of UV. Omalizumab was stopped due to non-improving symptoms. Cyclosporine was initiated, and shortly after, Dapsone was added due to improved but persistent symptoms. Normal G6PD levels were confirmed prior to starting treatment. Three weeks later, urticaria had resolved, however she developed tachycardia, dyspnea, and oxygen saturations of 87-90%. She was immediately sent to the hospital where was found to have methemoglobinemia (methemoglobin level: 25.9%) which was successfully managed with oxygen therapy. Urticaria did not recur. Dapsone was discontinued and Cyclosporine was tapered off.

Discussion: Management of UV often requires a multidisciplinary approach. First line agents consist of antihistamines and nonsteroidal anti-inflammatory drugs, and most patients respond to glucocorticoids. Recent cases have shown high rates of success with Omalizumab, especially in refractory cases. Our patient failed these treatments while responded to Dapsone, which is often used when symptoms persist; however, developed a potentially life-threatening adverse effect that is uncommonly seen without G6PD deficiency. This case highlights the importance of vigilant monitoring and consideration of potential adverse effects of therapy, including rare complications.

Anaphylaxis to Soy Chicken: A Case Report

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Background: Soybean is classified as a "Big Nine" allergen, accounting for a significant proportion of food allergies in Europe and the United States. Yet the heterogeneity of soybean products makes it all the more difficult – and crucial – to accurately diagnose and classify allergy to soybean.

Case Report: We present the case of a 5-year-old male with a history of mild cutaneous reactions to soy-containing products, who developed anaphylaxis after ingesting chicken nuggets containing soybean. The child initially presented to allergy clinic complaining of facial rash after exposure to soybean powder. Skin prick testing (SPT) was positive for soy at 8mm. He was advised to schedule a food challenge in the office but was lost to follow up. He continued to tolerate products with small amounts of soy lecithin. One year after his initial presentation, this child presented to the emergency room in anaphylaxis after ingesting 9 chicken nuggets containing soybean. Laboratory investigation revealed serum specific IgE to soy > 100kU/L. Soy components also resulted with Gly m 5, notably a diagnostic marker for being at high risk of severe clinical symptoms to soy; as well as Gly m 6 >100kU/L (see Figure 1). Gly m 4 was undetectable. Gly m 8 was not included in the panel. The patient was diagnosed with soy allergy, advised to strictly avoid soy-containing products, and prescribed an epinephrine autoinjector.

Conclusion: This patient case raises the complexity of soybean allergy and represents the population of individuals who tolerate traces of soy but may have fatal reactions to hidden allergens. Possible future plans for this case include clarifying what products the child has tolerated and considering food challenge to low dose soybean and/or soy lecithin.

An Observational Study of Environmental Allergy Skin Prick Testing versus Serum Antigen-Specific Immunoglobulin E Testing on Asthma Control and Maintenance

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Introduction: Identification of sensitizing inhalants with subsequent mitigation is an integral part of treatment in children with asthma. While both skin prick (SPT) or serum specific IgE (sIgE) tests can be used for this purpose, it is unclear whether either test are associated with better asthma control.

Methods: Pediatric patients with the diagnosis of asthma who underwent either SPT (N=29) or sIgE (N=26) testing were identified in the electronic medical record of the Los Angeles General Medical Center Allergy and Immunology Clinic between January 2020 and December 2023. Inclusion criteria were (1) confirmed diagnosis of asthma as determined by ICD-9 and/or ICD-10 codes; (2) age 2 to 18 years old; (3) patients with documented SPT or sIgE test; (4) minimum of 4 or more clinic visits in the year following either SPT or sIgE test. We followed patients from the time of their initial test and compared the number of visits until asthma control. We then compared the asthma control (as defined by NHLBI-EPR3 criteria) and maintenance of control after one year since initially achieving asthma control. 2-tailed t-tests, chi-square testing, and statistical analyses were performed in Minitab. Statistical significance was accepted at a p-value of less than 0.05.

Results: The mean number of visits until asthma control is reached for patients with SPT was 1.48 versus 2.15 in patients with sIgE testing (p= 0.065). With asthma control maintenance, 86.21% of patients who underwent SPT were able to maintain control of their asthma after one year since initially achieving control versus 65.38% of patients who underwent sIgE testing (p= 0.0695).

Conclusion: There was no difference in regards to time to achieving asthma and maintaining asthma between asthmatic children who received SPT versus sIgE testing. Both tests may be used to detect allergic sensitization in management of children with asthma

Case Study: Rash Evaluation and Drug Allergy Management in A Transplant Patient

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Background: The purpose of this case is to demonstrate rash evaluation and drug allergy management in a solid organ transplant patient on high dose steroid regimen when the workup has been unremarkable. Misdiagnosis of drug allergy in transplant patients may result in less appropriate medication use.

Case: A 62 year old African American male, with advanced COPD leading to bilateral lung transplant, presented with an erythematous maculopapular rash two months post-transplant. He was previously placed on numerous medications including Mycophenolate(500 mg BID), Tacrolimus (2 mg BID), Acyclovir (400 mg BID), Sofosbuvir-Velpatasvir (400-100 mg daily), Voriconazole (200 mg BID), Bactrim (800-160 mg three times/week), and Prednisone (10 mg daily). His skin exam was significant for post inflammatory changes and excoriations on the back, chest, and hands. Dermatological findings showed a generalized flat, polymorphic violaceous papular rash with pinpoint crusting, but no pustules or drainage. Skin biopsy indicated purpuric interface dermatitis with eosinophils, which suggested a drug reaction.
Laboratory evaluation/workup was unrevealing, and included normal liver and kidney function, negative rheumatological work-up, negative serology for Hepatitis/ HIV titers, Chagas disease, Toxoplasmosis, Syphilis, Strongyloides, Q fever, RMSF, CMV, EBV, Aspergillus fumigatus and Mycobacteria.
Confirming the diagnosis as a drug reaction was equivocal because the patient was admitted for worsening respiratory status secondary to rhinovirus infection and placed on 30 mg prednisone tapering. Bactrim and voriconazole were discontinued, with slow resolution of rash.

Discussion: A potential drug allergy was not confirmed due to his steroid regimen and a cause was never identified. Future patch testing will be considered with suspected medications once the patient is on prednisone (5 -10 mg) with subsequent oral drug challenge.

The association between classic IgE mediated food allergy and gluten sensitivity

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Introduction: Classic food allergy is mediated by the bonding of IgE antibodies to relevant food allergens. Gluten sensitivity with or without celiac disease, in contrast, is mediated by a non-humoral T-cell response to components of gluten. Previous studies have noted a significant association between severe food allergy and gluten sensitivity. In this study, we evaluated a possible association between classic food allergy and gluten sensitivity in a large all payers population.

Methods: This study is based on the Colorado all payers database (2017 to 2022). The patients were categorized by sex and age groups. Each patient in the data set has an ICD10 binary value to indicate whether he or she has gluten sensitivity and/or classic food allergy. We performed a statistical analysis using Python and its libraries (Pandas and SciPy) to assess the association between gluten sensitivity and classic food allergy. Results are reported in Odds Ratios (OR) and P values.

Results: Our study included 791,432 patients. Among them there were 367,727 (46.5%) males, and 423,705 (53.5%) females. We identified 2452 patients with classic food allergy and 931 patients with gluten sensitivity. They were categorized into 5 age groups: less than 18 years old (18.1%) , 18 to 29 (16.4%), 30 to 44 (24.8%), 45 to 64 (21.3%) and 65 and older (19.4%). In patients with food allergy, the risk of gluten sensitivity was significantly higher than in those without food allergy: OR 5.929 ($P < 0.0001$). For males: OR 4.452 ($P < 0.001$). For females: OR 6.891 ($P < 0.0001$). OR by age groups were as follows: OR 3.256 (<18, $P < 0.001$), OR 3.575 (18-30, $P< 0.001$), OR 18.481 (30-45, $P < 0.001$), OR 13.490 (45-65, $P < 0.001$) and OR 13.600 (>65, $P < 0.001$).

Conclusion: Our results indicate patients diagnosed with classic food allergy are at significantly increased risk for gluten sensitivity versus those without classic food allergy. We observed a somewhat stronger association among females than among males. Furthermore, the association was noticeably stronger in patients over age 30. Medical practitioners should have a low threshold for gluten sensitivity testing in patients with classic food allergy.