Eastern Allergy Conference
June 3-6, 2021 ~ Palm Beach, FL

Scientific Posters F1-F18 will be on display in the Ponce Exhibit Hall 1, 2, & 3, during the coffee break, 9:30-10:15am, Friday June 4th

Not for CME Credit

F1

Diagnostic and Treatment Implications of a Family with a Novel NFKB1 Variant

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We present a novel heterozygous NFKB1 variant manifesting as multisystem immune dysregulation.
A 19-year-old female with two-year history of Evans syndrome was treated with high-dose IVIG and steroids. At age 21, immune evaluation for bacterial (upper and lower respiratory), fungal, and viral (HSV and HPV) infections revealed agammaglobulinemia (undetectable IgG, IgA, IgM) and absent vaccination responses. T and B-cell phenotyping revealed low total and switched memory B-cells, expanded CD19hiCD21low and age-associated B cells (T-bet+ CD85j+ CD11c+) and low naïve CD4 T cell fraction (2.3% of total CD4). Lymphocyte proliferation (CD45 and CD3) to phytohemagglutinin was decreased. Blueprint 284-gene Primary Immunodeficiency Panel revealed novel likely pathogenic NFKB1 variant (c.162_163del, p.Gly55llefs*8) and two variants of undetermined significance in LRBA cis position. Consistent with loss-of-function phenotype of this novel NFKB1 variant, overexpression of mutant NFKB1 construct in vitro demonstrated reduced NFKB1 pathway signaling compared to wildtype by RNA-seq whole gene expression in Jurkat cells.
Clinical phenotype included CMV+ lymphocytic interstitial pneumonia (improved with ganciclovir and Cytogam), chronic granulomatous lymphocytic interstitial lung disease, lymphocytic liver disease, splenomegaly (treated with rituximab), and chronic enteropathy. We aim to improve overall Immune Deficiency and Dysregulation activity (IDDA) (Tesch JACI, 2020) of 28, with CTLA4-Ig therapy initiation. Hematopoietic stem cell transplant (HSCT) discussions have been initiated, although data on best conditioning regimen and outcomes are limited. Patient faces social barriers towards HSCT. Genetic testing of mother with history of ITP and hypogammaglobulinemia revealed identical NFKB1 variant.
Our case illustrates establishing the link between specific genetic defect and clinical phenotype facilitates multidisciplinary patient care with targeted therapy. Selecting best treatment approach (i.e. biologicals vs. HSCT) and optimal timing of administration is critical in improving outcomes of this rare condition. Finally, development of tools to monitor treatment response including clinical scoring and immune biomarkers is crucial and currently progressing.

F2

Chlorhexidine: An Important Cause of Perioperative Anaphylaxis

Nicholas C. Kolinsky, DO and Richard F. Lockey, MD

Identifying the culprit medication in cases of perioperative anaphylaxis can be extremely challenging. A detailed and accurate history, coupled with the appropriate testing, plays a key role in discovering the etiology of perioperative anaphylaxis. We present the case of a 48-year-old woman with a cranial meningioma who was scheduled for surgery. Chlorhexidine, midazolam, lidocaine, propofol, fentanyl, rocuronium, and furosemide were administered during the perioperative period. She developed hypotension, urticaria, bronchospasm, and other symptoms of anaphylaxis soon after general anesthesia. The serum tryptase level obtained during anaphylaxis was 119 ng/mL (normal, <11.4 ng/mL). Epinephrine was administered, and the surgery was canceled, with no cause identified. For the next surgical attempt, she was pretreated with diphenhydramine and ranitidine, and the neuromuscular blocker was withheld. Again, she developed hypotension consistent with anaphylaxis, and epinephrine was administered. She was referred for consultation. A detailed and accurate history was obtained. The baseline serum tryptase level was 6.4 ng/ml. Skin-prick puncture tests were completed, and a diagnosis was made. The surgical team was instructed to avoid the culprit medication, and the cranial surgery was successful. Although difficult, cases of perioperative anaphylaxis can be solved with a detailed history, keen detective work, and appropriate testing.

F3

Dupilumab Efficacy in Patients with Moderate-to-Severe Type 2 Asthma with and Without Elevated Blood Neutrophils

Eugene R. Bleecker, Reynold A. Panettieri, Njira L. Lugogo, Jonathan Corren, Nadia Daizadeh, Juby A. Jacob-Nara, Yamo Deniz, Paul J. Rowe, Angela Khodzhayev, Benjamin Ortiz, Thomas J. Ferro, Christopher N. Hansen

Introduction: Studies suggest disease outcomes in patients with type 2 inflammatory asthma, defined by elevated blood eosinophils (eos) or fractional exhaled nitric oxide (FeNO) levels, may worsen when blood neutrophils are elevated. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for IL4/13, key and central drivers of type 2 inflammation in multiple diseases. In the phase 3 QUEST study (NCT02414854), add-on dupilumab 200 mg and 300 mg every 2 weeks vs placebo significantly reduced severe asthma exacerbations and improved pre-bronchodilator forced expiratory volume in 1 second (FEV_1) in patients with uncontrolled, moderate-to-severe asthma. Treatment effects were greater in patients with a type 2 inflammatory phenotype. We evaluated the efficacy of dupilumab in QUEST patients with type 2 asthma, with and without elevated blood neutrophils at baseline.

Methods: We evaluated annualized severe exacerbation rates and change from baseline in pre-bronchodilator FEV_1 (L) at Week 52 in patients with type 2 asthma (type 2: eos ≥150 cells/μL or FeNO ≥20 ppb; type 2−high: eos ≥300 cells/μL or FeNO ≥50 ppb) and high (≥4,000 cells/μL) or low (<4,000 cells/μL) blood neutrophil counts at baseline.

Results: Of 1,902 QUEST patients, 1,582 were included in this post hoc analysis (type 2: 815 with ≥4,000 neutrophils/mL, 767 with <4,000 neutrophils/mL; type 2−high: 483 with ≥4,000 blood neutrophils/mL, 472 with <4,000 neutrophils/mL). Dupilumab significantly reduced annualized severe exacerbation rates (55–68% vs placebo; $P<0.001$ in all groups) and improved pre-bronchodilator FEV_1 at Week 52 (least squares mean difference vs placebo: 0.18–0.31 L; $P<0.001$ vs placebo in all groups), independent of type 2 status or neutrophil count.

Conclusions: Patients with both type 2 asthma and type 2−high moderate-to-severe asthma, with and without elevated blood neutrophil counts, demonstrated comparable reductions in annualized severe exacerbation rates and improvement in lung function upon treatment with dupilumab.

Funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

F4

Effect of Dupilumab Treatment on Blood Eosinophil Levels in Patients with Asthma, Chronic Rhinosinusitis With Nasal Polyps (CRSwNP), Eosinophilic Esophagitis (EoE), or Atopic Dermatitis (AD)

Michael E. Wechsler, Amy D. Klion, Pierluigi Paggiaro, Parameswaran Nair, Delphine Staumont-Salle, Amr Radwan, Robert Johnson, Upender Kapoor, Faisal A. Khokhar, Nadia Daizadeh, Zhen Chen, Elizabeth Laws[7], Juby A. Jacob-Nara, Leda Mannent, Marcella Ruddy, Paul J. Rowe, Yamo Deniz

Introduction: Dupilumab blocks the shared receptor component of interleukin-4/interleukin-13, key and central drivers of type 2 inflammation in multiple diseases. In patients with asthma or chronic rhinosinusitis with nasal polyps (CRSwNP), a transient increase in eosinophils was observed with dupilumab treatment. Eosinophil levels then declined over time, and the increase was rarely of clinical consequence. Here, we assess the effect of dupilumab treatment on blood eosinophil concentrations over time across indications.

Methods: Median percent change (95% CI) from baseline in blood eosinophil concentrations was measured in studies of dupilumab-treated patients with uncontrolled moderate-to-severe asthma (LIBERTY ASTHMA QUEST [NCT02414854]: N=1,902; TRAVERSE [NCT02134028] dupilumab/dupilumab arm: N=1,013); severe CRSwNP (SINUS-52 [NCT02898454]: N=303); eosinophilic esophagitis (NCT02379052: N=47); and moderate-to-severe atopic dermatitis (LIBERTY AD CHRONOS [NCT02260986]: N=425).

Results: In patients with asthma, blood eosinophils increased from baseline by 9.2% (4.3, 14.3; $P=0.001$) at Week 4, returned to baseline by Week 24, and fell below baseline by Week 52 (−12.3% [−15.9, −7.7]; $P=0.03$). This trend was sustained through Week 96 for dupilumab-treated patients who rolled over into the open-label TRAVERSE study. In CRSwNP, a 16.2% (−5.9, 34.0; $P=0.26$) rise was seen at Week 16 that resolved by Week 24. No rise was observed over the treatment period in eosinophilic esophagitis or atopic dermatitis. Hypereosinophilia (>3,000 cells/μL) was rare. Few patients discontinued dupilumab due to eosinophilia (QUEST: 7 discontinued in 52 eosinophilia cases, TRAVERSE: 2/3, SINUS-52: 1/2), and most cases did not require corrective treatment. Rare cases of eosinophilic granulomatosis with polyangiitis and eosinophilic pneumonia were reported; a causal association with dupilumab has not been established.

Conclusions: Transient early elevation of blood eosinophils in asthma or CRSwNP patients starting on dupilumab treatment generally declined to below baseline levels over time. Such increases were not seen in patients with eosinophilic esophagitis or atopic dermatitis.

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F5

Dupilumab Efficacy and Safety in Children with Uncontrolled Moderate-to-Severe Asthma: The Phase 3 VOYAGE Study

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Introduction: Asthma is the most common chronic respiratory condition in children. Type 2 inflammation underlies most childhood asthma cases. Dupilumab, a fully human mAb, blocks the shared receptor component for interleukin-4/interleukin-13, key and central drivers of type 2 inflammation in multiple diseases. VOYAGE, a 52-week (Wk) randomized, double-blind, placebo-controlled phase 3 study (NCT02948959), evaluated the efficacy and safety of dupilumab in children aged 6−11 years with uncontrolled, moderate-to-severe asthma.

Methods: Participants were randomized to add-on subcutaneous dupilumab 100mg or 200mg every 2 weeks (body weight ≤30kg or >30kg, respectively) or matched placebo in a 2:1 fashion. The primary-analysis populations were patients with the type 2 inflammatory asthma phenotype (baseline blood eosinophils ≥150cells/μL or FeNO ≥20ppb) and patients with baseline blood eosinophils ≥300cells/μL. Annualized severe asthma exacerbation rate (primary endpoint); change from baseline in pre-bronchodilator FEV_1 percent predicted (FEV_1pp) and FeNO at Wk12; and change in 7-item Asthma Control Questionnaire–Interviewer Administered (ACQ-7-IA) score at Wk24 were assessed. Safety was assessed in the safety population.

Results: 408 patients were randomized (type 2 inflammatory asthma phenotype: 350; blood eosinophils ≥300cells/μL: 259). In the type 2 population, dupilumab reduced the exacerbation rate (59.3%; P<0.0001); improved FEV_1pp (least squares [LS] mean difference vs placebo 5.21 percentage points; P=0.0009) and reduced FeNO (LS mean difference vs placebo −17.84ppb; P<0.0001) at Wk12. At Wk24, dupilumab improved ACQ-7-IA scores (LS mean difference vs placebo −0.33, P=0.0001). Similar findings were observed in patients with eosinophils ≥300cells/μL. Overall rates of treatment-emergent adverse events (TEAEs) with dupilumab (83%) and placebo (80%) were comparable. 13/271 (4.8%) dupilumab-treated and 6/134 (4.5%) placebo-treated patients reported serious TEAEs. 5/271 (1.8%) dupilumab-treated and 2/134 (1.5%) placebo-treated patients discontinued after an AE.
Conclusions: Dupilumab demonstrated efficacy and an acceptable safety profile in patients aged 6−11 years with uncontrolled, moderate-to-severe asthma with a type 2 inflammatory phenotype.

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F6

Reductions in asthma exacerbation-related hospitalizations and emergency department visits in patients with severe, uncontrolled asthma treated with tezepelumab: Results from the Phase 3 NAVIGATOR Study

Arnaud Bourdin, Andrew Menzies-Gow, Geoffrey Chupp, Elliot Israel, Åsa Hellqvist, Gillian Hunter, Christopher S Ambrose, Jean-Pierre Llanos-Ackert, Gene Colice, Bill Cook and Jonathan Corren[1]

Introduction
Tezepelumab is a human monoclonal antibody that blocks activity of thymic stromal lymphopoietin. In the phase 3 NAVIGATOR study (NCT03347279), tezepelumab significantly reduced exacerbations versus placebo (primary endpoint) in patients with severe, uncontrolled asthma. Secondary objectives of NAVIGATOR were the effects of tezepelumab on exacerbations that required hospitalization or an emergency department (ED) visit, and on asthma-related, unscheduled healthcare resource use.

Methods
NAVIGATOR was a multicenter, randomized, double-blind, placebo-controlled study. Patients (12-80 years old) receiving medium- or high-dose inhaled corticosteroids and ≥1 additional controller medication with or without oral corticosteroids, were randomized 1:1 to receive tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. The annualized rate of asthma exacerbations that required hospitalization (>24 hours in hospital) or an ED visit (<24 hours in an ED) over 52 weeks was assessed. Time to first exacerbation that required hospitalization or an ED visit and the proportion of patients who required asthma-related healthcare resources over 52 weeks were evaluated.

Results
Overall, 528 patients received tezepelumab 210 mg and 531 received placebo. Tezepelumab reduced the annualized rate of exacerbations that required hospitalization or an ED visit by 79% (95% CI: 63-88) versus placebo. Tezepelumab prolonged the time to first exacerbation that required hospitalization or an ED visit versus placebo; the risk reduction was 65% (hazard ratio [95% CI]: 0.35 [0.22-0.56]). Fewer tezepelumab-treated patients than placebo-treated patients required asthma-related hospitalizations (3.2% vs 7.0%), ED visits (4.4% vs 9.4%), unscheduled visits to a specialist (35.4% vs 43.5%), telephone calls with a healthcare provider (19.1% vs 25.0%) or ambulance transport (0.8% vs 2.3%).

Conclusions
Tezepelumab substantially reduced exacerbations that required hospitalization or an ED visit versus placebo. Tezepelumab-treated patients used less asthma-related healthcare resources than placebo-treated patients. This analysis further supports the benefits of tezepelumab in patients with severe, uncontrolled asthma.

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F7

Omalizumab for IgE-mediated food allergy: A systematic review and meta-analysis

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Introduction: Food allergy (FA) is an adverse immunologic response against food protein. We assessed changes in food tolerance, quality of life (QoL) when Omalizumab (OMA), a recombinant, humanized, monoclonal antibody against human immunoglobulin E (IgE) was used as monotherapy or as an adjunct to oral immunotherapy (OIT) in IgE-mediated FA.

Methods: We screened 868 records from literature databases, clinical trial registries for randomized controlled trial (RCT), controlled clinical trial (CCT) and observational studies using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Eight RCTs, 18 CCTs, 4 observational studies on OMA in adults, children with IgE-mediated FA that reported data on primary outcomes of interest were analyzed using pre-OMA, placebo as comparators. A meta-analysis of pooled estimates was conducted with Cochrane RevMan (v 5.3.5) and R software.

Results: OMA as monotherapy or as an adjunct to OIT was significantly ($P < 0.01$) associated in achieving tolerance for peanut (RR 6.34, 95% CI 1.00—40.06; RR 25.00, 95% CI 1.64—381.10), cow's milk (RR, 1.35, 95% CI 0.72—2.54; RR 3.00, 95% CI 0.15—60.88) allergy at 25, 30, 32, 139 weeks in RCT and CCT respectively, cow's milk and egg (RR 16.40, 95% CI 2.47—108.99) allergy at 13 weeks in CCT and multifood (RR 1.75, 95% CI 1.46—2.10; RR 18.18, 95% CI 2.65— 124.73; RR 7.33, 95% CI 3.61—11.05) allergy at 8—16, 12, 17 and 36 weeks in RCT, CCT and observational respectively. Overall, OMA as monotherapy or as an adjunct to OIT was associated with significant ($P < 0.01$) changes in QoL assessed using Food Allergy Quality of Life Questionnaire-Child and Teen Form (MD -2.11, 95% CI -2.83—-1.39) and Pediatric Quality of Life Inventory scale (MD 26.72, 95% CI 23.45—29.99) at 261 and 17 weeks in CCT and observational respectively.

Conclusion: Current evidence indicates OMA is associated with achieving tolerance to food allergen with a significant impact on QoL. Especially for severely affected patients, OMA is a good option to reduce the risk of anaphylactic reactions due to unexpected allergen contamination.

Funded by Genentech/Novartis

F8

Improved activity levels in patients with asthma: A post hoc analysis of omalizumab therapy

Brian Modena, Alison Greene, Jinnie Ko, Pranathi Janampally, Nayla Mumneh, Lauren A. Millette, Cecile T.J. Holweg, Diego J. Maselli

Rationale: Uncontrolled asthma may lead to exercise avoidance and decreased activity levels. Evidence suggests that exercise improves asthma control and quality of life (QoL), although this area is not well studied due to lack of standardized tools and metrics. Patients receiving omalizumab therapy for asthma show QoL improvements using the Asthma Quality of Life Questionnaire (AQLQ); therefore, we used the AQLQ activity limitation domain (ALD) to examine the impact of omalizumab on activity levels.

Methods: This post hoc study examined asthmatic patients from studies 008/009, INNOVATE (NCT00046748), EXTRA (NCT00314574), and PROSPERO (NCT01922037), separately. We assessed change from baseline in AQLQ ALD scores at the last study timepoint (Week 16, 28, 48, or end of study for 008/009, INNOVATE, EXTRA, and PROSPERO, respectively, or early termination). Reported results include: 1) least squares mean (LSM) (95% CI) differences (omalizumab-placebo), estimated using analysis of covariance; 2) descriptive statistics of outcomes for the single-arm PROSPERO study; and 3) the proportion of patients achieving a minimum clinically important difference (MCID; ≥0.5 points). ALD score is calculated as the average of 5 AQLQ ALD questions, each with a possible range of 1-7.

Results: LSM (95% CI) treatment difference (omalizumab-placebo) for change from baseline at study end in the ALD was higher for omalizumab-treated patients versus placebo in placebo-controlled studies: 008/009 (0.2 [0.1-0.4]), INNOVATE (0.5 [0.3-0.7]), and EXTRA (0.3 [0.1-0.4]). Mean (95% CI) change from baseline at study end/early termination in the open-label, real-world, single-arm PROSPERO study was 1.1 (1.0-1.2) points.
The proportion of patients achieving the MCID (≥0.5-point improvement) in AQLQ ALD was greater in omalizumab versus placebo groups (**Figure 1**). In PROSPERO, 67.5% (450/667) of omalizumab-treated patients achieved the MCID (≥0.5). The proportion achieving the MCID in PROSPERO was similar to that in other studies (**Figure 1**). Safety results have been published previously (Busse et al. *J Allergy Clin Immunol*. 2001; Solèr et al. *Eur Respir J*. 2001; Humbert et al. *Allergy*. 2005; Hanania et al. *Ann Intern Med*. 2011; Casale et al. *J Allergy Clin Immunol Pract*. 2019).

Conclusions: This analysis suggests that omalizumab treatment may positively impact activity levels levels—an important, yet understudied, outcome associated with improved asthma control. Whether this finding discovered in the context of a clinical trial translates to improved activity in daily life requires further exploration. Nonetheless, this finding signals the potential role of omalizumab therapy in supporting long-term health benefits related to increased exercise and activity levels.

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F9

Pregnancy and infant outcomes among pregnant women with Chronic Spontaneous Urticaria (CSU) treated with omalizumab: A descriptive analysis from the EXPECT pregnancy registry

Jennifer Namazy, MD; Angela E. Scheuerle, MD; Vic Spain, DVM, PhD; Pranathi Janampally; Ayesha Ahmed, PharmD; Sachin Gupta, MD; Cecile Holweg, PhD; Nayla Mumneh, MD; Cristine Radojicic, MD

Rationale: Treatment options for pregnant women with CSU are limited in patients who do not respond to high-dose antihistamine treatment as immunosuppressants are contraindicated during pregnancy. Omalizumab received FDA approval for antihistamine-resistant CSU, providing an alternative. Understanding pregnancy outcomes in women receiving omalizumab is important to guide continued treatment during pregnancy.

Methods: EXPECT was a prospective observational registry evaluating pregnancy outcomes in women receiving omalizumab (n=309) from 2006-2017. This post hoc analysis evaluated perinatal outcomes of 30 patients enrolled in EXPECT who received omalizumab for CSU during their pregnancy.

Results: All patients were exposed to omalizumab in the first trimester of pregnancy, with a mean duration of 11.8 months before enrollment; 70.0% (21/30) received omalizumab 300mg, and 86.7% (26/30) received monthly dosing. All pregnancies >20 weeks were live births. One spontaneous abortion (<20 weeks) occurred, and premature birth (<37 weeks) occurred in 13.3% (4/30) of pregnancies. Median (IQR) gestational age at delivery was 39.3 (39.0-40.3) weeks (mean 38.2 [SD 6]) for live births. Small for gestational age was not observed; 1 preterm infant had low birth weight. Two infants had major congenital anomalies: plagiocephaly resolved after 3 months of orthotic helmet use; mild pyelocaliectasis was resolved at 6-month follow-up.

Conclusions: Overall, the results of the present analysis were comparable to studies of patients with asthma in EXPECT where no increased risk was observed. Given the observational nature and low patient number in EXPECT, absence of increased risk with omalizumab in patients with CSU cannot be definitively concluded.

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F10

Physician Perspectives on Transitioning Long-Term Prophylactic Treatment in Patients with Hereditary Angioedema: Results from a Physician Survey

Douglas T. Johnston, Michael Steidle, Tam Khuu, Lindsey J Noble

Background: Hereditary angioedema (HAE) is a lifelong disease that is commonly treated with long-term prophylaxis (LTP). Multiple medications have gained FDA-approval for LTP of HAE over the past few years, each having unique characteristics and highlighting the need for patients and physicians to tailor treatment to individual needs and preferences. This survey seeks to evaluate factors influencing physician decision-making surrounding therapy transitions between LTP agents.

Methods: A 10-question internet survey was completed by 64 US-based physicians treating HAE (Allergists/Immunologists, A/I) between March and April 2021, prior to participation in a medical advisory board. Ninety-five (95%) percent of anonymous respondents (n=61 physicians) reported direct experience in switching LTP in ≥1 patient with HAE in the previous 12 months.

Results: A majority of respondents acknowledged having HAE management experience utilizing each currently available LTP agent, with ≥75% utilizing SC pdC1INH, lanadelumab-flyo, and berotralstat for LTP. The most important factors, as ranked by physicians, affecting the decision to switch LTP included: patient preference (73%), convenience of treatment (50%), and breakthrough attacks (48%). Most respondents re-evaluated patients 1-3 months after switching treatments to assess response. Physicians indicated maintenance of breakthrough attacks (81%), patient reported outcomes (i.e., quality of life) (59%) and utilization of on-demand medication (55%) as the most important factors when assessing success following an LTP switch.

Conclusions: Recently approved HAE LTP aim to control HAE attacks while increasing treatment convenience and decreasing treatment burden. Following a switch in LTP, physicians utilize a variety of parameters to evaluate response to the new LTP including HAE attack frequency, patient reported outcomes, and utilization of on-demand therapy. Results of this survey indicate the importance of shared decision-making to tailor individual treatment given that patient preference was ranked most important to physicians when considering a LTP switch.

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F11

Berotralstat consistently demonstrates reductions in attack frequency in Hereditary Angioedema (HAE) irrespective of baseline attack rate: Subgroup analysis from the APeX-2 Trial

H. Henry Li, Bhavisha Desai, Sharon Murray, Raffi Tachdijan

Rationale: Berotralstat is an oral plasma kallikrein inhibitor in development for HAE attack prophylaxis. HAE is characterized by unpredictable, episodic attacks; some patients experience frequent attacks without treatment. This analysis sought to understand whether baseline attack frequency correlates with responder rates with berotralstat.

Methods: 121 patients were randomized to berotralstat 110 mg:150 mg:placebo daily for 24 weeks in a phase 3 double-blind, placebo-controlled study (NCT03485911). This post hoc analysis examined the reduction of HAE attacks by baseline attack rate Cohort 1: < 2 attacks/month; Cohort 2: ≥2 to < 4 attacks/month; Cohort 3: ≥4 attacks/month.

Results: In Cohort 1, median baseline attack rates per month were 1.3 (berotralstat 150 mg; n= 10) and 1.7 (placebo; n= 12) which declined to 0.41 and 1.3, respectively. In Cohort 2, median baseline attack rates per month were 2.7 (berotralstat 150 mg; n=20) and 3.1 (placebo; n=21) which declined to 1.2 and 2.7, respectively. For Cohort 3, median baseline attack rates per month were 5.2 with berotralstat 150 mg (n=10) and 4.5 with placebo (n=6) and declined to 1.9 and 2.5, respectively. In Cohorts 1, 2, and 3, treatment with berotralstat 150 mg resulted in a ≥50% relative reduction in attack rate in 70%, 55%, and 50% of patients, respectively. In addition, 60%, 45%, and 50% of patients, respectively, had ≥70% relative reduction in attack rate.

Conclusion: These results demonstrate consistent responder rates with berotralstat, adding a potential oral prophylactic option to the treatment armamentarium for physicians.

Funded by BioCryst Pharmaceuticals, Inc.

F12

5-Period, 5-Treatment Crossover Study to Compare the Pharmacokinetics of Intranasal and Intramuscular Epinephrine Administration in Healthy Adult Participants

David Dworaczyk, PhD and Allen Hunt, MD[2]

Introduction: Intramuscular (IM) epinephrine via autoinjector has suboptimal compliance/use; alternatives are needed. We compared the bioavailability and cardiovascular effects of intranasal (IN) epinephrine nasal spray versus IM epinephrine.

Methods: This open-label, randomized, 5-treatment, 5-way crossover study included 25 healthy participants aged 19–45 years. Epinephrine administrations were: 6.6-mg IN (1x6.6-mg), 4.4-mg IN (2x2.2-mg), 8.8-mg IN (2x4.4-mg), 13.2-mg IN (2x6.6-mg), and 0.3-mg IM (1x0.3-mg); second IN administration within 10 seconds after first dose (opposite nostril); ≥1 day washout. Epinephrine concentrations and cardiovascular effects were measured (-30–360 minutes). Pharmacokinetic (PK) parameters evaluated included the area under the plasma concentration-time curve (AUC) from 0 to 10, 20, 30, 60, and 360 minutes (ie, $AUC_{0–10}$, $AUC_{0–20}$, $AUC_{0–30}$, $AUC_{0–60}$, $AUC_{0–360}$), maximum observed concentration from time 0 to 10 minutes ($C_{max[10\ min]}$) and C_{max}. PK parameters were analyzed by analysis of variance. Safety was assessed.

Results: Aside from AUC_{0-10}, AUCs and C_{max} values were greater after 6.6-mg IN versus 0.3-mg IM epinephrine ($AUC_{0–10}$, 936 vs 979 min*pg/mL; $AUC_{0–20}$, 3054 vs 2273 min*pg/mL; $AUC_{0–30}$, 5291 vs 3756 min*pg/mL; $AUC_{0–60}$, 10,171 vs 7433 min*pg/mL; $AUC_{0–360}$, 25,461 vs 15,163 min*pg/mL; $C_{max(10\ min)}$, 277 vs 246; C_{max}, 293 vs 238 pg/mL). After 20 minutes, baseline-corrected epinephrine concentrations ≥100 pg/mL were reached by 100% (13.2-mg IN), 80% (6.6-mg and 8.8-mg IN, 0.3-mg IM), and 60% (4.4-mg IN) of participants; epinephrine concentrations ≥200 pg/mL were reached by 64% (13.2-mg IN), 60% (6.6-mg IN), 56% (8.8-mg IN and 0.3-mg IM), and 32% (4.4-mg IN) of participants. IN epinephrine had no clinically meaningful heart rate/blood pressure effects.

Conclusions: Epinephrine bioavailability and cumulative PK data demonstrate that the single 6.6-mg IN epinephrine dose was comparable to or greater than dosing with the 0.3-mg IM epinephrine autoinjector, with similar cardiovascular effects.

Funded by Bryn Pharma, LLC

F13

Infections in Adults with Moderate-to-Severe Atopic Dermatitis Treated with Dupilumab: Long-Term Data from an Open-Label Extension (OLE) Study

Andrew Blauvelt, Andreas Wollenberg, Lawrence Eichenfiel, Zhen Chen, Ainara Rodriguez Marco, Jignesh Vakil, Faisal A. Khokhar, Sonya L. Cyr

Background: Atopic dermatitis (AD) is associated with immunologic and skin barrier dysfunction, predisposing patients to infections. Here, we report the incidence of infections in adults with moderate-to-severe AD treated with dupilumab for up to 3 years in an OLE study.

Methods: LIBERTY AD OLE (NCT01949311) is an ongoing trial assessing 300mg dupilumab weekly (higher than the approved adult dose [300mg every 2 weeks]) in adults with moderate-to-severe AD who participated in previous controlled dupilumab studies. Placebo+topical corticosteroids (TCS) and dupilumab 300mg weekly+TCS arms of the 52-week CHRONOS trial (NCT02260986) are provided for comparison because OLE lacks a control arm. CHRONOS was selected because it was the largest and longest controlled study where concomitant TCS was used. Infection data are based on the Medical Dictionary for Regulatory Activities search: Primary System Organ Class "Infections and Infestations;" incidence is reported as number of patients per 100 patient-years (nP/100PY).

Results: 2,677 patients were treated in OLE; 315 with placebo+TCS and 315 with dupilumab+TCS in CHRONOS. The overall exposure-adjusted incidence rate (nP/100PY) of infections in OLE (74.1) was lower than in CHRONOS placebo+TCS (107.0) and dupilumab+TCS (93.7) groups. The incidence of infections (nP/100PY) leading to treatment discontinuation (0.4) and serious/severe infections (1.4) in OLE was lower than CHRONOS placebo+TCS (0.9 and 2.1, respectively).

Conclusion: In comparison to the placebo arm of the 52-week CHRONOS trial, dupilumab 300mg weekly for up to 3 years in adults with moderate-to-severe AD was associated with a lower incidence of overall infections, serious/severe infections, and infections leading to treatment discontinuation.

Funded by Sanofi/Regeneron

F14

Dupilumab provides early and sustained clinically meaningful responses in a phase 3 trial in adolescents with inadequately controlled moderate-to-severe atopic dermatitis: Results from the overall population and in a subgroup of patients not achieving IGA scores of 0/1

Eric L. Simpson, Andrew Blauvelt, Emma Guttman-Yassky, Melinda Gooderham, Iftikhar Hussain, Zhen Chen, Noah A. Levit, Ana B. Rossi

Objective: We determined the proportion of atopic dermatitis (AD) patients with clinically meaningful responses following dupilumab treatment for 16 weeks in the overall adolescent population, and in a subgroup not achieving IGA scores of 0/1 at Week 16 (Wk16) in a double-blinded, phase 3 trial (LIBERTY AD ADOL: NCT03054428).

Methods: Adolescents with inadequately controlled moderate-to-severe AD were randomized 1:1:1 to subcutaneous dupilumab every 4 weeks (q4w; 300mg), every 2 weeks (q2w; 200 or 300mg), or placebo for 16 weeks. Clinically meaningful responses were defined as ≥50% improvement in EASI, or a ≥3-point improvement in weekly-averaged Peak daily Pruritus NRS, or a ≥6-point improvement in CDLQI from baseline through Wk16. A composite endpoint was defined as response in ≥1 of the above endpoints.

Results: Patients (N=251) were randomized to dupilumab q4w, q2w, and placebo. At Wk16, significantly more patients receiving dupilumab achieved the composite endpoint vs. placebo (q4w/q2w vs. placebo: 63.1%/80.5% vs. 23.5% [P<0.0001 for both]). Of 214 patients who did not achieve IGA 0/1 at Wk16, significantly more dupilumab-treated patients achieved the composite endpoint vs. placebo (q4w/q2w vs. placebo: 55.1%/74.2% vs. 21.7% [P<0.0001 for both]) at Wk16. Clinically meaningful responses were seen as early as Wk2 after first dupilumab dose. Dupilumab was generally well tolerated with an acceptable safety profile similar to that seen in the adult AD population.

Conclusions: A majority of adolescents treated with dupilumab, demonstrated early, progressive, and sustained clinically meaningful responses in ≥1 key AD domain compared with placebo.

Funded by Sanofi/Regeneron

F15

CAPTAIN Study: Effect of Baseline Lung Function on Response to Triple Therapy in Patients With Asthma Inadequately Controlled on Inhaled Corticosteroid/Long-acting β_2-agonist (ICS/LABA) therapy

Nathan R, Boulet L-P, Kerstjens HA, Papi A, Pavord ID, Hanania NA, Oppenheimer J, Maselli DJ, Liu MC, Weinstein S, Mannino D, Peachey G, Zarankaite A, Sule N, Fowler A, Lee L, Kerwin E

Introduction: The CAPTAIN study showed that adding umeclidinium (UMEC) to ICS/LABA **improves lung function and symptom control f**or patients with uncontrolled asthma, but the effects of UMEC may vary according to baseline lung function. We investigated the effect of UMEC addition on asthma outcomes according to baseline lung function.

Methods: CAPTAIN: Phase IIIA, randomized, double-blind, 24–52-week, parallel-group study in adults with uncontrolled asthma and airflow reversibility at screening. Treatment: fluticasone furoate (FF)/UMEC/vilanterol (VI) 100/31.25/25, 100/62.5/25, 200/31.25/25, 200/62.5/25mcg or FF/VI 100/25, 200/25mcg QD (ELLIPTA). Outcomes: change from baseline in clinic trough forced expiratory volume in 1 second (FEV_1) and asthma control questionnaire (ACQ)-7 response (≥0.5-point decrease from baseline) at Week 24, and annualized moderate/severe exacerbation rate according to baseline lung function subgroup: FEV_1 <60/≥60% predicted; FEV_1 reversibility to SABA <400/≥400 mL; FEV_1/forced vital capacity (FVC) ratio <0.7/≥0.7 (pre-specified exploratory analyses).

Results: UMEC addition improved trough FEV_1 in both FEV_1 <60/≥60% predicted subgroups, with FF/UMEC/VI 100/62.5/25 (n=207/197) resulting in improvements of 72mL (95% CI: 12, 132) and 146mL (84, 209), respectively, vs FF/VI 100/25 (n=210/192). FF/UMEC/VI 200/62.5/25 (n=188/219) led to improvements of 95mL (33, 157) and 88mL (28, 147), respectively, vs FF/VI 200/25 (n=201/200) in these subgroups. Trough FEV_1 improvements following UMEC addition to FF/VI 100/25 or 200/25 were also observed in both SABA reversibility and FEV_1/FVC subgroups. ACQ-7 responses favoring FF/UMEC/VI vs FF/VI were also observed across subgroups. FF/UMEC/VI 100/62.5/25 was associated with moderate/severe exacerbation rate reductions vs FF/VI 100/25 across subgroups. There was no clear pattern in treatment response on the rate of moderate/severe exacerbations according to baseline lung function for the FF-200 mcg dose comparisons.

Conclusions: The improvements observed following addition of UMEC to FF/VI, in both functional and clinical outcomes, were independent of baseline lung function.

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F16

CAPTAIN Study: Effects of Smoking Status on Treatment Response to Triple Therapy in patients with Inadequately Controlled Asthma on Inhaled Corticosteroid/Long-acting β_2-agonist (ICS/LABA) therapy

Papi A, Lee L, Kerstjens HA, Boulet L-P, Zarankaite A, Pavord ID, Brusselle G, Barnes N, Hanania NA, Pascoe S, Oppenheimer J, Pizzichini E, Fowler A

Introduction: In patients with uncontrolled asthma despite ICS/LABA, effects of adding a long-acting muscarinic antagonist (LAMA) or increasing ICS dose differ based on treatment outcome and may vary with smoking history. Therefore, we analysed effects of adding umeclidinium (UMEC) or increasing fluticasone furoate (FF) dose on forced expiratory volume in 1 second (FEV_1) and exacerbations by smoking status.

Methods: CAPTAIN: Phase IIIA, randomized, double-blind, 24–52-week, parallel-group study in adults with uncontrolled asthma and airflow reversibility at screening. Treatment: FF/UMEC/vilanterol (VI) 100/31.25/25, 100/62.5/25, 200/31.25/25, 200/62.5/25mcg or FF/VI 100/25, 200/25mcg QD (ELLIPTA). Outcomes: change from baseline in trough FEV_1 at Week 24 and annualized rate of moderate/severe exacerbations in former vs never smokers. Analyses were prespecified, except for the FF/VI 200/25 vs 100/25 comparison (post hoc in the smoking subgroups).

Results: Number of patients overall and for never smokers and former smokers, respectively: FF/UMEC/VI 100/62.5/25: 406, 325, 81; FF/UMEC/VI 200/62.5/25: 408, 315, 93; FF/VI 100/25: 407, 338, 69; FF/VI 200/25: 406, 337, 69. A numerical trend for greater reductions in exacerbation rates in former vs never smokers was seen for FF/UMEC/VI 100/62.5/25 vs FF/VI 100/25 and FF/UMEC/VI 200/62.5/25 vs FF/VI 200/25 (rate ratios [95% CI]: 0.55 (0.31–0.96) vs 0.86 (0.64–1.14); 0.69 (0.38–1.24) vs 1.06 (0.77–1.45), respectively). Effects of increasing ICS dose on exacerbations did not differ by smoking status. FEV_1 was improved by a greater extent in former vs never smokers following addition of UMEC 62.5mcg to FF/VI 100mcg or from doubling the FF dose in dual therapy (mean difference in change from baseline: 186mL (85–287) and 94mL (46–141) for FF/UMEC/VI 100/62.5/25 vs FF/VI 100/25; 142mL (36–247) and 33mL (-15, 80) for FF/VI 200/25 vs FF/VI 100/25.

Conclusions: Addition of UMEC was associated with a greater reduction in exacerbations in former vs never smokers, including with FF 200µg. For FEV_1, effects of both treatments were less consistent with smoking history.

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F17

Safety of Defatted Powder of *Arachis hypogaea* in Children and Teenagers With Peanut Allergy: Pooled Analysis From Controlled and Open-Label Phase 3 Trials

Kari R. Brown, A. Wesley Burks, James Baker, Brian P. Vickery, Thomas B. Casale

Introduction: Defatted powder of *Arachis hypogaea* (previously known as AR101) is an oral immunotherapy recently approved to mitigate allergic reactions following accidental peanut exposure in peanut-allergic individuals aged 4-17 years. Longer-term data will further characterize the adverse event (AE) profile of this treatment.

Methods: Safety data from six clinical trials (n=3, controlled; n=3, open-label extension) were pooled and assessed.

Results: Of the 1127 individuals receiving the treatment, totalling 1821 exposure-years, most participants experienced ≥1 AE(s) (n=1119; 99.3%). The maximum AE severity was mild for 410 participants (36.4%); moderate for 651 (57.8%), and severe for 57 (5.1%). One participant (0.1%) had a life-threatening AE unrelated to treatment (acute lymphoblastic leukemia). Serious adverse events occurred in 41 (3.6%) participants; of these, nine (0.8%) were treatment related. Overall, 150 (13.3%) participants discontinued due to AEs; most experienced a gastrointestinal symptom (n=93) and discontinued during the first 6 months (n=90). Exposure-adjusted AEs and treatment-related AEs occurred at a rate of 73.9 and 56.6 events/exposure-years, respectively, during updosing and decreased to 17.4 and 10.1 events/exposure-years, respectively, during 300-mg maintenance. Exposure-adjusted rates of anaphylactic reactions (eg, systemic allergic reactions of any severity) and epinephrine use were low during Year 1 (0.28 events/exposure-years and 0.26, respectively) and decreased in Years 2 (0.21 and 0.16) and 3 (0.13 and 0.10).

Conclusions: In this pooled safety analysis through 3 years of treatment, AEs decrease in frequency and severity of time, although the survivor bias should be taken into account. These data can aid clinicians in managing safety and facilitating shared decision-making.

Funded by Aimmune

F18

Rapid and Sustained Improvement in Itch in Children Aged 6–11 Years With Severe Atopic Dermatitis (AD) Treated With Dupilumab: Analysis From the LIBERTY AD PEDS Phase 3 Trial

Gil Yosipovitch, Jonathan I. Silverberg, Jashin J. Wu, Zhen Chen, Alvina Abramova, Randy Prescilla

Background: In LIBERTY AD PEDS phase 3 trial (NCT03345914) in children with severe AD, dupilumab significantly improved AD signs and symptoms. We assess time to onset of improvement in pruritus in a subset of children treated with FDA-approved doses of dupilumab.

Methods: Children aged 6–11 years were randomized to dupilumab 300mg every 4 weeks (300mg-q4w, loading dose 600mg), 100mg/200mg-q2w (loading dose 200mg/400mg), or placebo, with concomitant medium-potency topical corticosteroids (TCS). This analysis evaluated change from baseline in daily and weekly Peak Pruritus Numerical Rating Scale (PP-NRS) scores up to Week 16.

Results: This analysis included 243 patients treated with FDA-approved doses of dupilumab, or placebo (< 30kg: 600mg loading dose then 300mg-q4w+TCS/placebo+TCS; ≥ 30kg: 400mg loading dose then 200mg-q2w+TCS/placebo+TCS, n=61/61/59/62). The percent decrease in daily PP-NRS score (SE) from baseline of dupilumab+TCS vs placebo+TCS was significant, as early as Day 8 in the q4w group after a single dose (−13.8% [2.9] vs −5.1% [2.9]; $P < 0.05$) and Day 16 in the q2w group (−22.1% [3.4] vs −12.6% [3.3]; $P < 0.05$). At Week 16, mean percent change from baseline (SE) in weekly PP-NRS score in the q4w group vs placebo+TCS was −55.0% (4.0) vs −26.6% (4.3) ($P < 0.0001$) and −58.3% (4.0) vs −25.3% (3.9) ($P < 0.0001$) in the q2w group vs placebo+TCS. Safety profile was consistent with the known dupilumab safety profile.

Conclusions: Dupilumab + TCS treatment provided rapid and sustained improvement in itch intensity and frequency in children aged 6−11 years with severe AD.

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Eastern Allergy Conference
June 3-6, 2021 ~ Palm Beach, FL

Scientific Posters S1-S17 will be on display in the Ponce Exhibit Hall 1, 2, & 3, during the coffee break, 9:30-10:15am, Saturday June 5th

Not for CME Credit

S1

The other side of the coin: immunodysregulation in primary immunodeficiency. Analysis of the United States Immunodeficiency Network (USIDNET) database

Maria Chitty Lopez MD, Rahul Mhaskar MPH, PhD, Hannah Wright MSPH, Rebecca A. Marsh, MD, Elizabeth Garabedian MD, Ramsay Fuleihan MD, Kathleen E. Sullivan MD, Jennifer W. Leiding MD

Rationale: Substantial effort has been devoted to the characterization of infectious susceptibility in patients with primary immunodeficiencies diseases (PIDD). Non-infectious conditions especially immunodysregulation, autoimmunity, and auto-inflammation have been increasingly identified as major PIDD features. Our objective is to describe the frequency of immunodysregulatory conditions in a large US PIDD cohort.

Methods: The USIDNET is a national research consortium with 43 contributing academic and private centers.Data from PIDD patients is collected in a registry after obtaining informed consent. Patients were grouped by their diagnosis according to the IUIS 2019 classification. Immunodysregulatory conditions were categorized by affected organ system by investigators. The frequency of immunodysregulatory conditions and organ systems affected were determined within each IUIS category. The association between immunodysregulatory conditions and survival was investigated using a Chi-square or Fisher's exact test.

Results: 4,182 subjects with a diagnosis of PIDD were identified. The median age of diagnosis and median age of death (N=259) were 8 and 17 years respectively. Male to female ratio was 1.2:1. Analysis was performed on patients with known survival status (N=3,672). The majority of patients (57.8%) had one or more organ systems affected; 9.4% had 3 or more affected. Within IUIS categories, frequency of organ systems affected varied, the most common systems affected across the cohort were respiratory (30.6%), integumentary (19.3%), gastrointestinal (18.4%), immune (13.9%), and hematopoietic (11.5%). The most frequent IUIS categories to have immunodysregulatory conditions associated were Diseases of Immune Dysregulation (76.4%), and Defects of the Innate Immune System (73.0%). Specific immunodysregulatory conditions were more common within certain IUIS categories: hematologic dyscrasias (34.3%) were most common in Diseases of Immune Dysregulation, gastrointestinal conditions occurred most frequently (32.5%) in those within Congenital Defects of Phagocytes, and respiratory conditions (38.1%) were most common in Predominantly Antibody Deficiency. Immunodysregulatory conditions affecting cardiovascular ($p=0.014$), endocrine ($p=0.046$), gastrointestinal ($p<0.0001$), hematopoietic ($p<0.0001$), and immune systems ($p<0.0001$), were associated with death. Within each organ system affected, specific immunodysregulatory conditions were also associated with worse survival.

Conclusions: More than half of patients within our PIDD cohort had immunodysregulatory conditions associated with their diagnosis. Hematologic, GI, and respiratory conditions had the most negative effect on survival. This large cohort of patients were predominantly contributed by academic centers which may have influenced the observations towards more severe phenotypes. Given the high frequency of immunodysregulatory features, recognition of autoimmunity and auto-inflammatory symptoms should be used to guide surveillance strategies for recognition and diagnosis of PIDD.

S2

Noninvasive Yet Destructive Allergic Fungal Rhinosinusitis in an Immunocompetent Patient

Natalie Diaz-Cabrera, MD., Raul Villarreal, MD., Farnaz Tabatabaian, MD.

Introduction: Allergic fungal rhinosinusitis (AFRS) is caused by a hypersensitivity reaction to fungal allergens in atopic individuals, which can cause significant pathology.

Case description: A 15-year-old male presented to the emergency department for evaluation of acute onset headache and right eye protrusion. He endorsed a history of sinus pressure, nasal congestion, pain behind the right eye, and increased production of green discharge from the right nostril over the previous 6 months. His parents reported nasal polyps and seasonal environmental allergies controlled with cetirizine.

Labs showed WBC 13,000/uL with neutrophilic predominance to 12,100/uL and ESR 4 mm/hr. He had mild proptosis of the right eye on evaluation. Polyposis was identified on nasal speculum exam in the right nostril. CT sinus revealed hyperdense mucosal thickening of the right maxillary sinus with erosion of the medial wall and extension into the right ethmoid sinuses and right sphenoid sinus. MRI orbits w/w/o revealed dehiscence of bone along the inner wall of the frontal sinus, fovea ethmoidalis, and lamina papyracea on the right producing proptosis.

Management: Functional endoscopic sinus surgery was pursued. Nasal polyps and extensive mucinous secretions were seen bilaterally. Fungal culture grew *Curvularia* species and aerobic culture grew *Staphylococcus aureus*. Eosinophil count was greater than 100 eosinophils per high-power field on surgical pathology specimens. He was prescribed 20mg prednisone and intranasal fluticasone with improvement. Outpatient immunological evaluation revealed normal immunoglobulin levels,IgG subsets, and negative HIV screen. Tetanus and diphtheria antitoxoid antibody levels suggested appropriate response to immunization.

Discussion: AFRS due to *Curvularia* species in an immunocompetent host has been associated with extensive sinus destruction, central nervous system invasion, endocarditis, brain abscesses, skin infections, onychomycosis, endophthalmitis, pneumonia, and sinusitis. Patients experiencing neurological or ophthalmologic complications from sinusitis should have fungal cultures and smears taken. There is insufficient evidence regarding the efficacy of allergen immunotherapy in AFRS due to a lack of placebo-controlled trials. Surgical intervention followed by medical therapy has led to improved clinical outcomes compared to medical therapy alone.

S3

Anaphylactic Reaction to Chamomile Tea

Donya Imanirad, MD, Enrique Fernandez-Caldas, PhD, Richard F. Lockey, MD

Introduction: The family Asteraceae (Compositae) is one of the largest angiosperm families characterized by their composite flower heads that includes dog fennel and ragweed among many others.

Case: A 56-year-old male with allergic rhinitis and Hymenoptera hypersensitivity drank a cup with two tea bags of chamomile tea (Traditional Medicinals, Sebastopol, CA). Between 5 and 15 minutes of ingestion, he experienced pruritus of his oral pharynx, palms, and torso and developed urticaria on his thighs. Within 15 additional minutes he experienced tightness of his "throat" and felt he "could not breathe." He became hoarse and more short of breath and developed a feeling of impending doom. He self-administered Epipen, 0.3 mg, (Mylan Company, Canonsburg, PA.) into his thigh which he carries for Hymenoptera hypersensitivity and improved within 5-10 minutes. His problem resolved over the next hour or so. Prior history reveals that when he ate meals prepared with sunflower oil he developed generalized pruritus, and when a marigold garland was placed around his neck, he developed generalized pruritus and urticaria.
Each tea bag contains 1300 mg of chamomile flower and a warning: "Avoid this product if you are allergic to plants in the daisy (Astraceae or Compositae) family, such as chamomile or *echinacea*."
Prick puncture tests were 3-4+ positive to short ragweed, spiny pigweed, dog fennel, sheep sorrel, nettle, and English plantain. Lambs quarters was 4+ to an intradermal test. Sunflower, marigold flower, short ragweed and dog fennel are all in the Compositae family.
Chamomile pollen, *Matricaria recutita,* cross-reacts with the pollen of other members of the Compositae family, including mugwort (*Artemisia spp.*) and ragweed (*Ambrosia spp.*). SDS-PAGE gels reveal the presence of several bands in a wide range of molecular weights corresponding to different allergenic proteins.

Conclusion: This subject experienced anaphylaxis from chamomile tea, which contains allergens from the same botanical family to which he has positive skin tests. Subjects allergic to pollen in the Compositae family are susceptible to systemic allergic reactions and anaphylaxis secondary to the ingestion of chamomile tea.

S4

The Stubborn Rash

Stephanie N. Hudey*, M.D., Mark C. Glaum, M.D, Ph.D.

Introduction: Cutaneous T cell lymphoma presenting as suspected drug rash is described.

Case Description: A 64-year-old male with rheumatoid arthritis presents for evaluation of progressive skin rash. He initially notes diffuse xerosis three years prior, is diagnosed with eczema, and started on topical corticosteroids. One year later, rheumatology initiates methotrexate and he develops worsening skin rash. Given their concern for drug rash, methotrexate is stopped and he is trialed on adalimumab and sulfasalazine in succession, but the rash persists for greater than one year. It transiently improves with oral corticosteroid tapers. Skin biopsy while on adalimumab reveals superficial and deep perivascular and periadnexal lymphohistiocytic infiltrate with numerous eosinophils. Eight months later, he is evaluated by allergy. All medications are discontinued one month prior. Examination reveals pruritic, indurated plaques with nodularity on the trunk and upper extremities. CBC and CMP are unremarkable without eosinophilia. Repeat skin biopsy is performed given rash progression. It now reveals atypical lymphoid infiltrate, predominantly T cells with a preponderance of CD4+ variably sized cells. T cell β/γ gene rearrangement shows a monoclonal population. Oncology performs further evaluation with bone marrow biopsy, PET scan, and lymph node biopsy and he is diagnosed with stage IIB mycosis fungoides with large cell transformation. He is initiated on INF-α with total skin external beam radiation therapy.

Discussion/Lessons Learned: This case demonstrates the importance of including cutaneous T cell lymphoma in the differential diagnosis of rashes that may be encountered by allergists in clinical practice. It also stresses the need to reconsider the diagnosis and repeat skin biopsy for rashes that fail to respond to conventional treatment or evolve in appearance.

S5

Dupilumab Reduces Need for Systemic Corticosteroids, Sinonasal Surgery in Patients With Severe Chronic Rhinosinusitis With Nasal Polyps: Pooled Results From SINUS-24, SINUS-52 Phase 3 Studies

Martin Desrosiers, Claus Bachert, Peter Hellings, Claire Hopkins, Heidi Olze

Introduction: Current treatment paradigm for chronic rhinosinusitis with nasal polyps (CRSwNP) is characterized by recurrent surgeries and/or frequent systemic corticosteroid (SCS) use. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, key drivers of type 2 inflammation. Dupilumab efficacy and safety were evaluated in patients with severe CRSwNP in two phase 3 studies, SINUS-24 (NCT02912468) and SINUS-52 (NCT02898454). This prespecified analysis evaluates the effect of dupilumab on SCS use and nasal polyp (NP) surgery in patients with CRSwNP previously treated with SCS and/or surgery receiving mometasone furoate in a pooled SINUS-24/-52 population.

Methods: SINUS-24 patients were randomized 1:1 to subcutaneous (SC) dupilumab 300 mg or placebo every 2 weeks (q2w) for 24 weeks. SINUS-52 patients were randomized 1:1:1 to 52 weeks of SC dupilumab 300 mg q2w, 24 weeks q2w then every 4 weeks for 28 weeks, or 52 weeks of placebo q2w. This pooled analysis included all patients randomized to dupilumab 300 mg q2w (n=438) and placebo (n=286) over the 24- and 52-week treatment periods. Kaplan-Meier method was used to estimate probabilities of events up to Week 52.

Results: Baseline disease characteristics were comparable between groups. 74.3% of patients used SCS in the past 2 years; 63.4% had prior NP surgery. Dupilumab vs placebo significantly reduced proportion of patients requiring SCS rescue by 73.9% (hazard ratio [HR] 0.261, 95% CI 0.18-0.38; P<0.0001), number of SCS courses by 75.3% (HR 0.247, 95% CI 0.17-0.37; P<0.0001), and need for NP surgery by 82.6% (HR 0.174, 95% CI 0.07-0.46, P=0.0005). Common adverse events (≥5%) were nasopharyngitis, NP, headache, asthma, epistaxis, and injection-site erythema, all occurring with higher frequency in placebo-treated patients.

Conclusions: Dupilumab significantly reduced SCS use and NP surgery in patients with severe CRSwNP in the pooled SINUS-24/SINUS-52 population and was well tolerated.

Funded by Sanofi and Regeneron Pharmaceuticals, Inc

S6

Dupilumab Efficacy in Patients With Chronic Rhinosinusitis With Nasal Polyps by History of Prior Sinonasal Surgery: Pooled Results From the SINUS-24 and SINUS-52 Phase 3 Studies

Claire Hopkins, Joseph K. Han, Stella E. Lee, Jerome Msihid, Amr Radwan[5]

Introduction: Chronic rhinosinusitis with nasal polyps (CRSwNP), a type 2 inflammatory disease, is often treated with surgery when severe or refractory, but nasal polyp (NP) recurrence is common. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor for interleukin (IL)-4/IL-13, key and central drivers of type 2 inflammation in multiple diseases. We report dupilumab efficacy in patients with CRSwNP from the SINUS-24 (NCT02912468) and SINUS-52 (NCT02898454) trials by number of prior NP surgeries and time since last surgery.

Methods: Subgroup analyses were performed for dupilumab 300mg every 2 weeks and placebo in patients with 0/1/2/≥3 prior surgeries (n=265/254/94/111) and patients who had surgery within <5/5–10/≥10 years (n=217/133/108).

Results: Lund–MacKay (LMK), nasal congestion (NC), and smell (University of Pennsylvania Smell Identification Test [UPSIT]) scores were worse in patients with prior surgery vs no surgery, but NP score (NPS) was lower; P < 0.05 for all. NPS was more severe with a longer time since surgery (P<0.0001), but NC and UPSIT were similar across groups. Dupilumab improved all outcomes at Week 24 regardless of the number of prior surgeries (least squares [LS] mean difference vs placebo for 0/1/2/≥3 surgeries: NPS −1.75/−2.02/−2.06/−2.10; NC −0.71/−0.94/−0.95/−1.09; LMK −5.73/−5.91/−7.11/−6.76; UPSIT 10.45/11.04/12.13/8.71; sino-nasal outcomes test (SNOT-22) −15.64/−21.13/−20.75/−19.95) or years since last surgery (LS mean difference vs placebo for <5/5–10/≥10 years: NPS −2.45/−1.66/−1.31 [subgroup interaction for <5 vs ≥10 years: P<0.01]; NC −1.07/−0.84/−1.00; LMK −7.89/−6.08/−3.94 [subgroup interaction for <5 vs ≥10 years: P<0.0001]; UPSIT 11.60/10.35/8.31; SNOT-22 −21.38/−23.74/−16.14).

Conclusions: Dupilumab improved all CRSwNP outcomes regardless of the number of prior surgeries or time since last surgery, with more recent surgery associated with a better baseline NPS.

Funded by Sanofi and Regeneron Pharmaceuticals, Inc.

S7

Indirect treatment comparison of biologics used for the treatment of chronic rhinosinusitis with nasal polyps

Anju T. Peters, Joseph K. Han Peter Hellings, Enrico Heffler, Philippe Gevaert

Introduction: Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) experience high disease burden despite treatment with systemic corticosteroids or sinus surgery. Randomized clinical trials (RCTs) of anti-interleukin (IL)-4/IL-13 (dupilumab) and anti-immunoglobulin E (omalizumab) demonstrated efficacy in CRSwNP versus intranasal corticosteroids (INCS). In the absence of head-to-head data between biologics, an indirect treatment comparison (ITC) was performed.

Methods: Embase®, MEDLINE®, and CENTRAL were searched for studies in adults with CRSwNP uncontrolled on INCS. Bucher ITCs were performed for Week-24 endpoints: nasal polyp score (NPS) 0–8, nasal congestion (NC) 0–3, loss of smell (LoS) 0–3, University of Pennsylvania smell identification test (UPSIT) 0–40, total symptoms score (TSS) 0–12, sino-nasal outcomes test (SNOT-22) 0–110, and responders based on NPS or NC improvement ≥1.

Results: Four phase 3 RCTs qualified for inclusion: dupilumab SINUS-24/52 (NCT02912468/NCT02898454); omalizumab POLYP1/2 (NCT03280550/NCT03280537). Qualitative assessment of trial design, baseline characteristics, and outcome measures used suggested that patient populations were comparable. In the intent-to-treat population, Bucher ITCs demonstrated that dupilumab had significantly greater improvements from baseline to Week 24 versus omalizumab in NPS, NC, LoS, UPSIT, and TSS; improvement in SNOT-22 was greater in dupilumab versus omalizumab but was not statistically significant. Dupilumab patients were significantly more likely to achieve ≥1-point improvement in NPS and NC versus omalizumab.

Conclusions: Dupilumab had consistently greater improvements in key CRSwNP outcomes versus omalizumab at Week 24. Although ITCs have limitations, in the absence of head-to-head studies these results can be useful for decision-makers.

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S8

Reduction in Severity Following 12 Months of Epicutaneous Immunotherapy for Peanut Allergy

Philippe Bégin, J. Andrew Bird, Jonathan M. Spergel, Dianne E. Campbell, Todd D. Green, Katharine J. Bee, Romain Lambert, Hugh A. Sampson, David M. Fleischer

Introduction: Daily epicutaneous immunotherapy (EPIT) for 12 months with DBV712 250 µg has been shown to be statistically superior to placebo in desensitizing (increasing reactivity threshold) 4-11-year-old peanut-allergic children in a Phase 3 clinical trial (PEPITES). While decreasing the likelihood of accidental ingestion reactions through desensitization is a major goal of food allergy immunotherapy, caregivers and patients also desire a reduction in reaction severity.

Methods: Double-blind, placebo-controlled food challenges (DBPCFC) were performed at baseline and following treatment (Month-12) to determine eliciting dose (ED) in PEPITES. Standardized DBPCFCs were stopped only after sufficient objective signs/symptoms, in accordance with PRACTALL guidelines. Symptoms in each body system were graded by prespecified criteria. Maximum severity of symptoms at baseline and Month-12 between active and placebo groups was compared post-hoc, in all organ systems (AOS) and five significant symptom domains (5SS) of wheezing, cardiovascular, laryngeal, vomiting and diarrhea.

Results: At baseline, there was a similar proportion of mild/moderate/severe objective signs/symptoms in AOS systems (P= 0.931) and 5SS systems (P=0.946) between DBV712 250 µg and placebo. At Month-12, there was a significant difference between groups in AOS and 5SS organs systems severity, irrespective of ED (P<0.001 and 0.016, respectively). By AOS, 16.2% of active subjects had a maximum symptom severity of "severe" compared with 27.5% in placebo (P=0.019). Similarly, at Month-12, 20.7% of active subjects had no 5SS symptoms compared with 11% of placebo (P=0.031).

Conclusions: In addition to increasing reactivity threshold in 4-11-year-old peanut-allergic children, investigational EPIT with DBV712 250 µg may also reduce the severity of allergic reactions.

Funded by DBV Technologies

S9

An evaluation of factors influencing response to epicutaneous immunotherapy for peanut allergy in the PEPITES trial

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Introduction: Epicutaneous immunotherapy (EPIT) for peanut allergy is a potential novel immunotherapy that utilizes unique cutaneous immunologic properties to desensitize. A randomized, double-blind, placebo-controlled Phase 3 trial (PEPITES) in peanut-allergic children 4-11 years demonstrated an epicutaneous patch (DBV712) with 250µg peanut protein was statistically superior to placebo in inducing desensitization following 12 months of daily treatment. The objective of this study is to investigate baseline and in-study factors influencing DBV712 250µg response, with focus on patch adhesion, by post-hoc analysis of PEPITES data.

Methods: Post-hoc multivariate model built with log-transformed Month 12 eliciting dose (ED) as dependent variable was used to assess influence of baseline characteristics and patch adhesion. Baseline characteristics and treatment response also evaluated by stratifying subjects into decile subgroups by patch detachment rates over the 12-month study.

Results: Multivariate analysis identified higher baseline ED, lower peanut-specific IgE as variables most predictive of higher Month 12 ED, followed by mean daily patch application duration, baseline SCORing Atopic Dermatitis (SCORAD) score, and age. By decile stratification, no association between patch detachment and treatment response was identified for 80% of DBV712-treated subjects. All DBV712-treated subjects, including those with highest patch detachment rates, demonstrated treatment benefit measured by fold-changes in geometric mean ED.

Conclusion: Higher baseline ED and lower baseline peanut-specific IgE were most predictive of higher Month 12 ED. For most treated subjects, patch detachment did not impact treatment response. A minority, highly sensitive to peanut at baseline, had lower pre-specified responder rates and higher patch detachment rates, yet still benefited from treatment based upon fold-changes in ED.

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Evaluation of daily patch application duration for epicutaneous immunotherapy for peanut allergy

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Introduction: The efficacy of an epicutaneous patch (DBV712) with 250 µg peanut protein applied once daily for 12-months in peanut-allergic children 4-11 years old has been previously demonstrated. We assessed the relationship between daily application duration and efficacy for DBV712 250µg.

Methods: DBV712 250µg was applied to 30 nonallergic volunteers for various durations from 2-24 hours, then assayed for residual peanut protein. Patch application data from the Phase 3 clinical trial were analyzed post-hoc according to pre-specified responder rates and changes in eliciting dose (ED), using geometric mean (GM) ED ratio (12 months/baseline).

Results: Median peanut protein remaining on the patch decreased from 2 to 12 hours of application and was below limit of quantification after 12 hours. Median daily patch application duration in the Phase 3 trial was 21.1 hours (DBV712 250µg) and 22.4 hours (placebo). 95% of the treated population achieved >10 hours per day mean application. For subjects with mean range of patch application duration from >10 hours to >20 hours, the pre-specified responder rate ranged from 36.6%-42.6%, with GM ED ratios of 3.8 to 4.0, respectively. In DBV712 250µg subjects with >16 hours mean application duration (84.5% of treated population), the responder rate was 38.8% versus 13.4% for placebo (difference, 24.4% [95% CI, 15.5%-34.0%, P<0.001]).

Conclusion: Evaluation of residual peanut protein on patches and post-hoc analysis of Phase 3 data strongly suggest that allergen delivery is attained with at least 12-16 hours of daily patch application time, sufficient to drive clinically meaningful desensitization to peanut after 12 months.

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S11

Twice-daily Administration of Exhalation Delivery System With Fluticasone and Patient Satisfaction

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Introduction: International guidelines recommend intranasal corticosteroids (INS) to improve symptoms and patient-reported outcomes in chronic rhinosinusitis with and without nasal polyps (CRSwNP/CRSsNP). Exhalation delivery system with fluticasone (EDS-FLU) delivers INS high and deep in the nasal passages (ie, ostiomeatal complex). Though the recommended dosage of most conventional INS is twice daily (BID) and evidence suggests that topical INS BID may offer better efficacy than once daily (QD) for patients with CRSwNP, INS may be used (or are prescribed) QD or less. A survey was conducted regarding the use of EDS-FLU to examine the correlation between QD, BID, or not-daily use with patient satisfaction.

Methods: Patients prescribed EDS-FLU were surveyed to assess how often they used EDS-FLU (BID, QD, not daily) and how satisfied they were with EDS-FLU. Patients rated their satisfaction on a 5-point Likert scale, with “satisfaction” defined as 4 or 5.

Results: Of 224 patients identified as having received an EDS-FLU prescription, 73 with CRSwNP and 48 CRSsNP consented to respond. Of the patients responding (N = 121), 67 reported using EDS-FLU BID, 39 reported QD, and 15 reported infrequent use (less than daily). More patients using EDS-FLU BID indicated satisfaction with EDS-FLU compared with patients using EDS-FLU QD (76% vs 59%). Only 40% of patients who reported infrequent use of EDS-FLU were satisfied. The number of patients using EDS-FLU BID who reported satisfaction was similar among patients with CRSwNP and CRSsNP ([77%] and [74%], respectively). Also, fewer patients with CRSwNP or CRSsNP expressed satisfaction when they infrequently used EDS-FLU ([50%], and [36%], respectively).

Conclusions: More patients with CRS who used EDS-FLU twice daily reported satisfaction compared with patients using EDS-FLU once daily or less. This real-world evidence is consistent with prior studies of INS showing that twice daily administration provides more reliable efficacy compared with once daily.

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S12

Real-world Effectiveness of Benralizumab on Asthma Exacerbations: Results from the ZEPHYR 1 Study

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Rationale: Although randomized clinical trials have demonstrated the impact of benralizumab on reducing asthma exacerbations, there are few studies describing the impact of benralizumab on asthma exacerbations in a real-world setting. This is one of the first studies to characterize US patients taking benralizumab in a real-world setting and to identify the impact on asthma exacerbations.

Methods: This retrospective cohort study utilized data from a large medical and pharmacy claims data source between November 2016 and November 2019. A pre-post design was implemented, in which the index date was the day after benralizumab initiation. Eligible patients initiating benralizumab were diagnosed with asthma, aged ≥12 years at index, biologic-naïve in the pre-index period, had 24 months of continuous insurance enrollment, and had ≥2 asthma exacerbations in the pre-index period. The primary cohort focused on patients with ≥2 records of benralizumab, and a secondary cohort examined persistent benralizumab users (≥6 records of benralizumab including the index record in the 12 months post-index). Asthma exacerbations in the 12-month periods pre- and post-index were analyzed and compared using generalized estimating equations.

Results: Among the 204 patients in the primary cohort with ≥2 records of benralizumab, the mean age at index was 45.3 years old, 68.6% were female, 45.1% had commercial medical insurance, and 40.7% had Medicaid. The most common pre-index comorbidities included allergic rhinitis (77.5%), mental disorders (49.5%), and hypertension (45.6%). Additionally, 33.8% of patients had chronic sinusitis, 30.9% of patients had chronic obstructive pulmonary disease, and 16.7% of patients had nasal polyps. Almost all patients used oral corticosteroids at some point during the pre-index period (99.0%), and the majority of patients had also used inhaled corticosteroids with long-acting beta-agonists (77.9%) and leukotriene modifiers (83.3%). The rate of asthma exacerbations decreased with statistical significance from 3.25 exacerbations per person-year in the pre-index period to 1.47 exacerbations per person-year in the post-index period, representing a 55% reduction (p<0.001). Furthermore, 41% of patients had no exacerbations in the post-index period. Greater exacerbation reductions were observed among persistent benralizumab users (n=103), with a statistically significant 62% reduction (3.23 asthma exacerbations per person-year pre-index to 1.23 asthma exacerbations per person-year post-index, p<0.001), and 43% of patients had no exacerbations in the post-index period.

Conclusion: Patients treated with benralizumab in this real-world analysis experienced a significant reduction in asthma exacerbations consistent with the reduction observed in the pivotal randomized clinical trials of benralizumab.

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S13

Mepolizumab for Chronic Rhinosinusitis With Nasal Polyps: Comorbid Asthma, NSAID Exacerbated Respiratory Disease, Eosinophil Stratification

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Introduction: SYNAPSE, a Phase III study, assessed the efficacy and safety of mepolizumab in chronic rhinosinusitis with nasal polyps (CRSwNP). Additional stratification by comorbid asthma, non-steroidal anti-inflammatory drug exacerbated respiratory disease (N-ERD), and baseline blood eosinophil count (BEC) was required.

Methods: SYNAPSE (NCT03085797), a randomized, double-blind, placebo-controlled, multicenter, 52-week study, included patients with recurrent severe bilateral CRSwNP and CRS symptoms. Patients received intranasal corticosteroids and met criteria for revision surgery. Change in total endoscopic NP score and nasal obstruction visual analog scale (VAS) score (co-primary endpoints) and time-to-first nasal surgery (key secondary endpoint) were analyzed by comorbid asthma, N-ERD, and (post hoc) baseline BEC.

Results: In patients with/without comorbid asthma, mepolizumab (n=140/66) versus placebo (n=149/52) efficacy (adjusted difference in median change from baseline [95% CI]) was similar for endoscopic NP score at Week 52 (-1.00 [-1.40,-0.60]/-0.42 [-0.98,0.13]) and nasal obstruction VAS score at Weeks 49–52 (-2.88 [-3.97,-1.79]/-3.12 [-5.23,-1.02]); patients receiving mepolizumab without comorbid asthma had fewer surgeries than patients with comorbid asthma (hazard ratio [95% CI]: 0.18 [0.05,0.64]) versus 0.61 [0.32, 1.15]). For patients with/without comorbid N-ERD, mepolizumab (n=45/161) versus placebo (n=63/168) improvements in endoscopic NP score (-0.89 [-1.73,-0.05]/-0.50
[-0.89,-0.11]) and reductions in surgery risk (0.32 [0.11,0.89]/0.47 [0.24,0.92]) were similar; improvements with mepolizumab compared with placebo in nasal obstruction VAS score were greater in patients with N-ERD than patients without N-ERD (-4.43 [-5.82,-3.03]/-2.42 [-3.67,-1.18]). Improvements across endpoints trended higher with BEC ≥150 versus <150 cells/µL.

Conclusions: Mepolizumab was generally efficacious irrespective of comorbid asthma or N-ERD; patients without comorbid asthma had fewer surgeries, patients with N-ERD had greater improvements in obstruction VAS score. Mepolizumab efficacy increased with higher BEC. Results suggest mepolizumab is efficacious for treating CRSwNP, particularly in patients with BEC ≥150 cells/µL.

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S14

Impact of baseline clinical asthma characteristics on the response to mepolizumab: a post hoc meta-analysis of two Phase III trials

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Introduction: Severe asthma is associated with a broad range of phenotypes. We assessed whether select baseline clinical characteristics could influence the efficacy of mepolizumab in patients with severe eosinophilic asthma (SEA).

Methods: This was a post hoc meta-analysis of data from the Phase III MENSA and MUSCA studies. Patients aged ≥12 yrs with SEA and ≥2 exacerbations were randomized to 4-weekly placebo or mepolizumab 100 mg subcutaneously for 32/24 weeks (MENSA/MUSCA). We assessed: annual rates of clinically significant exacerbations (primary endpoint); proportions of patients achieving complete asthma control (Asthma Control Questionnaire [ACQ]-5 score <0.75); changes from baseline in pre-bronchodilator forced expiratory volume in 1 second (FEV_1), St George's Respiratory Questionnaire (SGRQ) total score, and ACQ-5 score. Analyses were performed by: age at asthma onset (<18/18–40/≥40 years); lung function (% predicted FEV_1 ≤60/60–80/>80%), airway reversibility (≥12/<12% change in FEV_1), and asthma control (uncontrolled vs partial/complete control [ACQ-5 score ≥1.5/<1.5]) at baseline.

Results: Overall, 936 patients received mepolizumab or placebo. Across age, lung function, and airway reversibility subgroups, mepolizumab reduced exacerbation rates by 49–63% versus placebo. FEV_1, SGRQ total score, and ACQ-5 score were also improved with mepolizumab versus placebo across the majority of age and lung function subgroups. Patients were more likely to achieve complete asthma control with mepolizumab versus placebo, irrespective of baseline asthma control (odds ratio mepolizumab/placebo [95% confidence interval]: 2.28 [1.47,3.54] and 2.31 [1.38,3.87] for baseline ACQ-5 scores ≥1.5 and <1.5).

Conclusions: Mepolizumab is beneficial for patients with SEA who have a broad range of baseline clinical characteristics.

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S15

Managing Patients with Severe Asthma and Common Comorbidities of Atopy, Obesity & Depression/Anxiety: Real-world Effectiveness of Mepolizumab

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Introduction: Mepolizumab has been shown to improve severe asthma control in clinical trials. However, physicians treat holistically and consider comorbid conditions when selecting therapy. Atopy, obesity, and depression/anxiety affect patients with asthma at an increased rate, yet few studies have examined asthma therapy with these comorbidities. This study examined the impact of mepolizumab in patients with severe asthma and atopy, obesity or depression/anxiety.

Methods: Retrospective claims database analysis of patients with commercial/Medicare supplemental insurance with asthma, ≥12 years of age at mepolizumab initiation (index date), ≥2 mepolizumab administrations 6 months post-index, ≥12 months of continuous enrollment before (baseline) and after (follow-up) the index date, and a medical claim for one of the pre-specified comorbidities during baseline. Asthma exacerbations and OCS-use were compared between baseline and follow-up periods for each of the non-mutually exclusive comorbid subgroups.

Results: Patient subgroups were identified with the following comorbidities: Atopy (N=468); Obesity (N=171); Depression/Anxiety (N=173). After initiating mepolizumab, the mean rate of exacerbations was reduced in all groups: 48% in atopy, 52% in obesity, 38% in depression/anxiety ($p<0.0001$). All subgroups also had significant decreases in mean number of OCS claims (atopic 33%; obesity 38%; depression/anxiety 31%; $p<0.001$) and OCS bursts (atopic 40%; obesity 48%; depression/anxiety 37%; $p<0.001$) compared to baseline.

Conclusions: This study demonstrates that patients with asthma and atopy, obesity or depression/anxiety have significantly fewer exacerbations and reduced OCS use in a real-world setting following treatment with mepolizumab. Holistic patient care for severe asthma is critical and mepolizumab provides tangible clinical benefit despite the complexities of medical comorbidities.

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S16

Recombinant Human C1 Esterase Inhibitor as Short-Term Prophylaxis During Dental Surgery in a 5-Year-Old With Hereditary Angioedema

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Introduction: Recombinant human C1 esterase inhibitor (rhC1-INH) is indicated in the US for the treatment of acute attacks of hereditary angioedema (HAE) in adolescents/adults, and in the European Union for patients aged ≥2 years. rhC1-INH is administered using weight-based dosing (<84 kg, 50 U/kg; ≥84 kg, 4200 U). HAE attacks, characterized by disabling and painful swelling, are generally unpredictable, but triggers can include dental/medical procedures. A preemptive management plan for patients with HAE can minimize the attack risk. Global HAE guidelines recommend short-term prophylaxis with C1-INH concentrate, administered as close as possible to initiation of the procedure.

Methods: We present the case report of a child with HAE due to C1 inhibitor deficiency who received rhC1-INH as short-term prophylaxis to prevent potential breakthrough HAE attacks during dental surgery.

Results: A male with a paternal history of HAE was diagnosed with type I HAE at age 3 years. He had no other medical conditions and was not receiving long-term prophylaxis. At age 4.8 years, he needed to have several dental crown repairs/cavities addressed, which would require undergoing anesthesia and intubation. Given that he had not previously undergone a major medical procedure, and the planned procedure invasiveness, including intubation, we recommended short-term prophylaxis to reduce the risk of an HAE attack. The child (weight, ~17 kg at time of surgery), was prescribed rhC1-INH 50 U/kg (850 U) the night before the procedure and rhC1-INH 50 U/kg (850 U) to be administered 30−60 minutes prior to beginning the outpatient dental procedure. He tolerated the anesthesia and dental procedure well, and no HAE attacks were reported through at least 7 days post-procedure. No adverse effects related to rhC1-INH administration were observed.

Conclusions: Short-term prophylaxis with rhC1-INH prior to a dental procedure appeared efficacious and safe in a child <5 years of age with HAE.

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The Efficacy and Safety of Dupilumab in Adult and Adolescent Patients With Eosinophilic Esophagitis: Results From Part A of a Randomized, Placebo-Controlled Three-Part, Phase 3 Study

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Objective: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4/IL-13. Part A of a three-part, randomized, placebo-controlled phase 3 study (NCT03633617) evaluated the efficacy and safety of weekly dupilumab 300 mg vs placebo in adult and adolescent EoE patients for 24 weeks.

Methods: 81 patients received dupilumab (n=42) or placebo (n=39). Co-primary endpoints: proportion of patients achieving a peak esophageal intraepithelial eosinophil (eos) count of ≤6 eos/high-power field (hpf), and absolute change from baseline in Dysphagia Symptom Questionnaire (DSQ) score at Week 24. Secondary endpoints: percent change in peak esophageal intraepithelial eos count, absolute change from baseline in total EoE Endoscopic Reference Score (EREFS), proportion of patients achieving peak eos count < 15 eos/hpf, and change from baseline in gene expression as measured by normalized enrichment score (NES), using the EoE diagnostic panel (EDP) or type 2 inflammatory genes.

Results: Baseline characteristics were comparable between groups. At Week 24, a higher proportion of dupilumab-treated vs placebo-treated patients achieved a peak eos count of ≤6 eos/hpf (59.5% vs 5.1%, P<0.001) and <15 eos/hpf (64.3% vs 7.7%, P<0.001). Dupilumab-treated patients had greater percent change from baseline in peak eos count (LS mean difference −68.26% [95% CI −86.90 to −49.62]), greater change in DSQ score (−12.32 [−19.11 to −5.54]), and greater change in total EREFS (−2.9 [−3.91 to −1.84]) vs placebo (all P<0.001). Dupilumab, but not placebo, suppressed EDP NES and type 2 inflammation NES. Dupilumab was well tolerated; the most common TEAEs for dupilumab vs placebo were injection-site reactions (16.7% vs 10.3%) and nasopharyngitis (11.9% vs 10.3%).

Conclusion: In this phase 3 study, dupilumab demonstrated significant and clinically meaningful improvements in histologic, symptomatic, endoscopic, and molecular aspects of EoE, and was well tolerated with an acceptable safety profile.

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