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Dupilumab Improves Nasal Polyp Burden and Asthma Control in Patients With CRSwNP and NSAID-ERD

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Background: Dupilumab, a fully human anti-interleukin (IL)-4R α monoclonal antibody, inhibits signalling of IL-4/IL-13, key drivers of Type 2 inflammation, and is approved for treatment of adults with inadequately controlled, moderate-to-severe atopic dermatitis. In a phase 2a study (NCT01920893), dupilumab improved endoscopic, radiographic, and clinical endpoints in patients with chronic rhinosinusitis with nasal polyposis (CRSwNP) refractory to intranasal corticosteroids. This post hoc analysis evaluates the effect of dupilumab in CRSwNP patients with difficult-to-treat comorbid Nonsteroidal Anti-Inflammatory Drug-Exacerbated Respiratory Disease (NSAID-ERD).

Method: Sixty adults with CRSwNP were assigned to weekly subcutaneous 300mg dupilumab or placebo plus mometasone furoate nasal spray for 16 weeks. Nasal Polyp Score (NPS), Lund-MacKay (LMK) score, Smell Identification Test (UPSIT), 22-item Sino-Nasal Outcome Test (SNOT-22), AM nasal congestion/obstruction scores, 5-item Asthma Control Questionnaire (ACQ-5) score, and forced expiratory volume in 1 second (FEV1) were assessed at baseline and Week 16

Results: In 19 patients with CRSwNP and NSAID-ERD (11 placebo, 8 dupilumab), dupilumab showed significant improvements vs placebo in all sino-nasal outcomes assessed ($P<0.05$), including NPS (least-squares mean change [SE] -2.48 [0.53] vs 0.81 [0.55] for placebo), LMK score (-11.86 [2.90] vs -4.72 [3.23]), SNOT-22 score (-30.14 [4.53] vs -5.76 [4.66]), AM nasal congestion/obstruction score (-1.03 [0.18] vs -0.18 [0.19]), UPSIT (9.98 [4.63] vs -7.26 [5.81]), and in asthma outcomes assessed ($P<0.05$), including ACQ-5 (-1.17 [0.26] vs 0.19 [0.20]) and FEV1 (0.38L [0.11] vs 0.01L [0.11]).

Conclusion: Dupilumab significantly improves sino-nasal disease, asthma control, and lung function in a difficult-to-treat CRSwNP patient subgroup with comorbid NSAID-ERD.

Funded by: Sanofi Regeneron

Type 2 Biomarkers Associated with Dupilumab Efficacy in Patients with Uncontrolled, Moderate-to-Severe Asthma Enrolled in the Phase 3 Study LIBERTY ASTHMA QUEST

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Introduction: Dupilumab, a fully human IL-4R α monoclonal antibody inhibiting IL-4/IL-13, key drivers of Type 2 inflammation, is approved for the treatment of adults with moderate-to-severe atopic dermatitis (AD). In a double-blind, parallel-group, phase 3 study (NCT02414854), adults and adolescents with uncontrolled, moderate-to-severe asthma on standard-of-care controller therapy, received add-on 200/300mg dupilumab every 2 weeks or matched-placebo for 52 weeks. Dupilumab significantly reduced severe exacerbation rates and improved pre-bronchodilator forced expiratory volume in one second (FEV1). These post hoc analyses evaluate associations between baseline Type 2 inflammatory biomarkers and therapeutic responses to dupilumab.

Methods: Interactions between baseline levels of Type 2 biomarkers, including fractional exhaled nitric oxide (FeNO), eosinophils, periostin, IgE, and eotaxin-3, and dupilumab were determined for annualized severe exacerbation rate using un-penalized negative-binomial regression spline modeling and for change from baseline in FEV1 at Week 12 using un-penalized regression spline modeling.

Results: In 1,902 patients, significant treatment-by-baseline biomarker interactions with severe exacerbation rate were observed for eosinophils ($P<0.0001$) and FeNO ($P<0.0001$), and with FEV1 for eosinophils ($P<0.0001$), FeNO ($P<0.0001$), periostin ($P<0.0009$), IgE ($P<0.0245$), and eotaxin-3 ($P<0.0151$). The most frequent adverse event with 200/300mg dupilumab vs placebo was injection-site reactions (15%/18% vs 5%/10%). In contrast to dupilumab studies in AD, conjunctivitis adverse events were similar between groups.

Conclusions: Multiple Type 2 biomarkers showed significant treatment interactions with FEV1 (eosinophils, FeNO, periostin), and severe exacerbations (eosinophils, FeNO), suggesting different biologic pathways for lung function and exacerbations. Eosinophils and FeNO are common to both, and may be better biomarkers for asthma management.

Funded by: Sanofi Regeneron

Dupilumab Reduces Exacerbations and Improves Lung Function in Uncontrolled, Moderate-to-Severe Asthma Patients Across Prior Historical Exacerbation Subgroups in the Phase 3 LIBERTY ASTHMA QUEST Study

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Background: Dupilumab, a fully human anti-interleukin (IL)-4R α monoclonal antibody that inhibits IL-4/IL-13, key drivers of Type 2 inflammation, is approved for treatment of adults with inadequately controlled, moderate-to-severe atopic dermatitis (AD). In a double-blind, placebo-controlled phase 3 study (NCT02414854), asthmatics aged ≥ 12 years, without a minimum baseline eosinophil requirement, uncontrolled with medium-to-high-dose inhaled corticosteroids plus up to two additional controllers, received add-on dupilumab 200/300 mg or matched placebo every 2 weeks for 52 weeks. Both dupilumab regimens significantly reduced annualized severe exacerbation rates during the treatment period, improved pre-bronchodilator forced expiratory volume in 1 second (FEV1) at Week 12, and were generally well tolerated. This post hoc analysis assessed the efficacy of dupilumab by the number of exacerbations experienced prior to the study.

Methods: Annualized severe exacerbation rates during the treatment period and change from baseline in pre-bronchodilator FEV1 at Week 12 were analyzed in patient subgroups with ≥ 1 , ≥ 2 , ≥ 3 , or ≥ 4 prior-year exacerbations.

Results: Both dupilumab doses vs placebo reduced severe exacerbations over the treatment period ($P<0.01$) and improved FEV1 at Week 12 ($P<0.01$), regardless of prior exacerbation history; greater reductions in severe exacerbations were observed as prior exacerbation history increased. The most frequent adverse event (AE) occurring at higher frequency in the dupilumab-treated groups vs placebo was injection-site reactions (15%/18% vs 5%/10%). Conjunctivitis AEs were similar between dupilumab and placebo.

Conclusion: Dupilumab significantly reduced severe exacerbations and improved FEV1 regardless of exacerbation history, with generally greater improvements as prior exacerbation history increased, in patients with uncontrolled, moderate-to-severe asthma.

Funded by: Sanofi Regeneron

Dupilumab Improves All ACQ-5 Individual Items in Patients with Chronic Rhinosinusitis with Nasal Polyposis (CRSwNP) and Asthma: Results from a Phase 2a Trial

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Introduction: Dupilumab, a fully human anti-interleukin (IL)-4R α monoclonal antibody, inhibits signaling of IL-4/IL-13, key drivers of Type 2 inflammation, and is approved for treatment of inadequately controlled, moderate-to-severe atopic dermatitis. In a phase 2a study (NCT01920893), dupilumab improved endoscopic, radiographic, and clinical endpoints in patients with chronic rhinosinusitis with nasal polyposis (CRSwNP) and asthma. Dupilumab effect on each of 5 items of the Asthma Control Questionnaire (ACQ-5) was evaluated in patients with CRSwNP and asthma.

Methods: Adults with CRSwNP refractory to intranasal corticosteroids were assigned to weekly subcutaneous 300 mg dupilumab or placebo, with twice daily 200 μ g mometasone furoate nasal spray. Asthma control was assessed using ACQ-5 scores at baseline and at Week 16.

Results: Of 60 enrolled patients, 58.3% had asthma and used asthma medications. Dupilumab showed clinically relevant improvements vs placebo in total ACQ-5, with significant reductions in each of 5 items assessing asthma symptoms, including shortness of breath (least squares mean change [SE] -1.33 [0.27] vs -0.29 [0.29] for placebo), wheezing time (-1.5 [0.34] vs -0.54 [0.36]), awake in the morning with symptoms (-1.46 [0.20] vs 0.01 [0.22]), activity limitation (-0.93 [0.21] vs -0.11 [0.23]), and night-time awakenings (-0.91 [0.23] vs 0.08 [0.24]). Asthma control improvement correlated with improvements in rhinosinusitis visual analogue scale, 22-item Sino-Nasal Outcome Test, and nasal polyposis score. Injection-site reactions, headache, and nasopharyngitis were the most frequently reported adverse events with dupilumab.

Conclusion: In CRSwNP patients with asthma, dupilumab significantly improved all asthma-related items. Improvement correlated with reduced nasal polyp burden.

Funded by: Sanofi Regeneron

Increased risk of Angioedema with concomitant use of ACE-inhibitors and DPP-4 inhibitors.

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Introduction: Hypertension (HTN) and type 2 diabetes (T2DM) are common conditions among U.S. adults. Angiotensin converting enzyme inhibitors (ACE-Is) are frequently used to treat HTN and are associated with bradykinin-mediated angioedema. T2DM management often requires multiple oral agents, including newer anti-hyperglycemic drugs such as dipeptidyl peptidase 4 inhibitors (DPP4-Is). Although the risk of angioedema with DPP4-Is alone has not been extensively studied, this risk is increased with concomitant use of ACE-Is.

Objective: To present a case of angioedema in a patient on an ACE-I, after initiating a DPP4-I.

Methods: Case report

Results: A 67 year old female with HTN, T2DM, and no drug allergies presented to the clinic after several hours of lower lip swelling. She denied associated tongue/throat swelling, respiratory or abdominal complaints, new foods, or insect bites prior to symptom onset. Vital signs were normal and her exam was notable for asymmetric lower lip edema (R>L). She was on Lisinopril (ACE-I) for several years, and 3 weeks prior to presentation was started on Sitagliptin (DPP4-I). The Lisinopril was discontinued and the Sitagliptin continued. Her angioedema subsequently resolved.

Conclusion: The concurrent use of ACE-I and DPP4-I block two major pathways of bradykinin and substance P degradation, leading to elevated levels of both. This poses a greater risk of angioedema compared to the ACE-Is alone. Increased awareness of this drug-drug interaction may prevent potential harm.

Response to Omalizumab Observed Over Wide Range of Blood Eosinophil Levels

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Introduction: Inclusion criteria for efficacy studies of asthma biologics have resulted in highly enriched patient populations. Applying comparable methods, we examined response to omalizumab using different baseline blood eosinophil cut-points to facilitate selection of patients most likely to derive the greatest clinical benefit from therapy.

Methods: This post hoc analysis included patients with moderate or severe persistent allergic asthma from the 16-week inhaled corticosteroid dose-stable phase of two phase III clinical trials of omalizumab. For this analysis, asthma exacerbations were defined as the number of events requiring ≥ 3 days of systemic corticosteroids. Asthma exacerbation rates for omalizumab versus placebo were evaluated with respect to baseline blood eosinophil counts using a wide range of cut-points ($\geq 0, 100, 200, 300, 400/\mu\text{L}$) to define subgroups. *P*-values and 95% confidence intervals (CI) for comparisons of exacerbation rates were calculated using unadjusted negative binomial models.

Results: A total of $N=1071$ adults and adolescents (≥ 12 years) were randomized to receive either omalizumab ($n=542$) or placebo ($n=529$). The overall relative exacerbation rate reduction for omalizumab versus placebo was 57% (95% CI, 34–71%; $P<0.001$). Exacerbation rate reductions were significant across a wide range of eosinophil levels: ≥ 0 : 56% (95%CI 33%, 71%; $P=0.0002$), ≥ 100 : 57% (95%CI 33%, 72%; $P=0.0002$), ≥ 200 : 55% (95%CI 25%, 73%; $P=0.002$), ≥ 300 : 67% (95%CI 36%, 84%; $P=0.001$), ≥ 400 : 74% (95%CI 40%, 88%; $P=0.001$).

Conclusions: In patients with moderate or severe persistent allergic asthma, response to omalizumab is observed across a wide range of eosinophil levels.

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Impact of baseline IgE levels on exacerbations and asthma symptom control after omalizumab initiation

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Introduction: Immunoglobulin E (IgE) is important in asthma pathogenesis; omalizumab is the only biologic to specifically target IgE, with dosing in asthma customized to IgE levels. However, confusion abounds as to whether IgE is a biomarker for response.

Methods: Patients ≥ 12 y/o identified as omalizumab candidates by their treating physicians and with access to treatment through insurance or other funding were enrolled in PROSPERO ($n=801$); US-based, multicenter, prospective, 48-week observational study of patients with allergic asthma initiating treatment with omalizumab. Asthma-related exacerbations and Asthma Control Test (ACT) scores were recorded over 48 weeks. Outcomes were analyzed by baseline IgE level in 100IU/mL intervals (<100 to >700).

Results: At baseline, median (range) IgE levels were 193.3IU/mL (1.1-68,628). Patients reported mean (SD) 3.0 (3.28) exacerbations in the 12 months prior to study entry and 0.78 (1.37) exacerbations at the end of the study. Reductions in exacerbations were consistent regardless of baseline IgE levels (Spearman's corr. = -0.05, $p=0.18$). Patients reported poorly controlled asthma at baseline, mean (SD) ACT 13.94 (4.98), which improved to 18.37 (4.85) at the end of the study irrespective of IgE levels (Spearman's corr. = 0.06, $p=0.08$). Average change in ACT exceeded the minimal important difference (3) in all IgE subgroups. Adverse events were consistent with the safety profile described in the current product label.

Conclusions: In a real-world setting, patients treated with omalizumab had improved asthma control with decreased asthma exacerbations and increased ACT scores regardless of baseline IgE levels suggesting that, although important in omalizumab dosing, IgE may not be a predictive biomarker for response to omalizumab.

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Recurrent anaphylaxis caused by alpha gal allergy

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Introduction: Alpha-gal allergy represents a form of allergy to carbohydrate galactose-alpha-1,3-galactose found in mammalian meat. The sensitization to the carbohydrate occurs through the saliva of the lone star tick bite, which causes delayed allergic reactions.

Case Information: A 46 year old female was referred for evaluation of recurrent episodes of anaphylaxis since 2007. Her symptoms occur 3- 6 hours after meals including: diaphoresis, skin flushing, generalized pruritus, urticarial rash, chest tightness, and lightheadedness with no clear triggers. She has no known food or medication allergies. She had reported tick bites in the past. All her labs were normal including negative skin prick to both environmental and food allergens. The patient had a tentative diagnosis of idiopathic anaphylaxis and was prescribed an epipen. From 2007- 2012, the patient continued to have episodes of unexplained nocturnal anaphylaxis that required the use of epipen. In 2012, she suspected that eating beef or pork at dinner triggered her anaphylaxis. At that time, the diagnosis of Alpha-gal allergy was entertained, and was then confirmed by an Alpha gal IgE showing significant elevation at 4.13 KU/L (normal level < 0.35). After being advised to avoid mammalian meat, the patient did not experience any anaphylaxis. Her alpha-gal IgE level normalized to 0.23 KU/L in June 2017.

Summary: Alpha-gal allergy syndrome includes the non-protein epitope causing the anaphylaxis present in mammalian meats. The delayed nature of the reaction, and the sensitization by an agent seemingly unrelated to the ultimate trigger (lone star tick).

Prevalence and Patterns of Food Allergy Among School Children of Eastern North Carolina

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Introduction: Food allergy (FA) is a growing problem for U.S. Schools with almost one in thirteen children being affected. A significant number of them suffer from severe allergic reactions, which can be life threatening.

Methods: We analyzed the most recent FA data (through July 2017) of 23674 students from Pre-K to 12th graders in 43 schools (23 elementary, 13 middle, 7 high schools) in Eastern North Carolina. We obtained this data from the school health program at Vidant Medical Center in Greenville, NC. We looked at the prevalence of physician diagnosed FA and its pattern amongst those students.

Results: Number of students (NOS) with Physician diagnosed FA: 1506/23674 (6.36%).

Peanut: 24.18%, Tree nut: 15.69%, Shellfish 10.65%, Egg 6.79%, Milk 6.38%, Fish 5.62%, Wheat 3.04%, Soy 2.57%, Other 25.05%.

NOS with multiple food allergies: 160/1506 (10.62%).

NOS with a history of severe reactions: 184/1506 (12.2%).

NOS who carry Epinephrine: 233/1506 (15.5%).

NOS with FA Action Plan: 149/1506 (9.89%).

Conclusion: The prevalence of FA in our sample was 6.36%, approximately the same as the national average. Children with a history of severe food reactions make up 12.2% of diagnosed children. The percentages of students who carry Epinephrine and have Action plans are low, at less than 16% and 10% respectively. This reflects the need of health education in order to effectively plan for, recognize, and respond to an allergic reaction.

Clinical Efficacy of Benralizumab in Patients With Severe, Uncontrolled Eosinophilic Asthma and Nasal Polyposis: Pooled Analysis of the SIROCCO and CALIMA Trials

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Introduction: Nasal polyposis (NP) has been associated with an eosinophilic asthma phenotype and may predict benralizumab's efficacy.

Methods: *Post-hoc* pooled analysis of the Phase III SIROCCO (48 weeks; *Lancet*. 2016;388:2115–27) and CALIMA (56 weeks; *Lancet*. 2016;388:2128–41) trials. Patients aged ≥ 12 years receiving high-dosage ICS/LABA with baseline blood eosinophils ≥ 300 cells/ μ L received benralizumab 30 mg SC every 8 weeks (Q8W; n=506) or placebo (n=515).

Results: Patients with NP (NP⁺) generally had greater mean blood eosinophil counts (Q8W: 668 cells/ μ L; placebo: 749 cells/ μ L) than patients without NP (NP⁻; Q8W: 606 cells/ μ L; placebo: 597 cells/ μ L). Baseline maintenance OCS use was also greater for NP⁺ (Q8W: 31.3%; placebo: 21.4%) than NP⁻ (Q8W: 10.5%; placebo: 10.1%). Placebo exacerbation rates during treatment were 1.27 (n=515), 1.74 (n=117), and 1.13 (n=398) for the overall, NP⁺, and NP⁻ groups, respectively. Compared with placebo, benralizumab Q8W reduced exacerbation rates by 42% for all patients (rate ratio [RR], 0.58 [95% CI, 0.48–0.70], $p < 0.001$; n=506), by 54% for NP⁺ (RR, 0.46 [95% CI, 0.31–0.69], $p < 0.001$; n=115), and by 38% for NP⁻ (RR, 0.62 [95% CI, 0.50–0.78], $p < 0.001$; n=391); and increased prebronchodilator FEV₁ by 0.128 L for all patients (95% CI, 0.064–0.191, $p < 0.001$; n=502), by 0.272 L for NP⁺ (95% CI, 0.124–0.421, $p < 0.001$; n=115), and by 0.102 L for NP⁻ (95% CI, 0.032–0.172, $p = 0.004$; n=387). Similar trends were observed for efficacy measures of asthma symptoms (ACQ-6) and asthma-related quality of life (AQLQ[S]+12).

Conclusion: Benralizumab demonstrated enhanced clinical efficacy for patients with severe, uncontrolled eosinophilic asthma and NP.

Funded by: AstraZeneca

Seasonal Variability of Exacerbations in Patients With Severe, Uncontrolled Eosinophilic Asthma and Clinical Benefits of Benralizumab: Pooled Analysis of the SIROCCO and CALIMA Trials

Lawrence DuBuske, Paul Newbold, Yanping Wu, Frank Trudo

Introduction: Benralizumab is an anti-eosinophilic antibody with demonstrated efficacy for patients with severe, uncontrolled eosinophilic asthma. This study evaluated seasonal variation in the frequency of asthma exacerbations and the reduction of exacerbations with benralizumab treatment for patients with severe, uncontrolled eosinophilic asthma.

Methods: This was a *post-hoc* analysis of pooled data from the Phase III SIROCCO (*Lancet*. 2016;388:2115–27; [N=1,204]) and CALIMA (*Lancet*. 2016;388:2128–41; [N=1,091]) trials of patients aged 12–75 years receiving high-dosage inhaled corticosteroids/long-acting β_2 -agonists (ICS/LABA). Patients received benralizumab 30 mg SC every 4 weeks (Q4W) or every 8 weeks (Q8W; first three doses Q4W) or placebo. The primary analysis population was patients receiving high-dosage ICS/LABA with baseline blood eosinophils ≥ 300 cells/ μ L. The primary efficacy endpoint was the rate of asthma exacerbations.

Results: The observed crude rates of exacerbations for patients with severe, uncontrolled eosinophilic asthma were greater for fall and winter (1.52 and 1.44, respectively) compared with spring and summer (1.11 and 1.02, respectively) for the placebo-treated group. The annual percentage exacerbation rate reduction by season for benralizumab Q8W vs. placebo were spring, 50% ($p < 0.001$); summer, 45% ($p < 0.001$); fall, 46% ($p < 0.001$); and winter, 40% ($p < 0.001$). Similar trends were observed for patients receiving benralizumab Q4W.

Conclusions: Benralizumab treatment significantly reduced the frequency of exacerbations compared with placebo in patients with severe, uncontrolled eosinophilic asthma, and this reduction was consistent, with a 40–50% reduction irrespective of the season.

Funded by: AstraZeneca

High-Resolution Geographic Mapping of Severe Uncontrolled Asthma Data Regionally Across the United States

Eugene Bleeker, Hitesh Gandhi, Ileen Gilbert, Geoffrey Chupp

Introduction: Emerging data demonstrating substantial heterogeneity among severe asthma phenotypes has led to precise therapies that improve outcomes and a debate about the definition and scope of severe uncontrolled asthma (SUA). We compared public-domain US morbidity/mortality statistics with county/city prescription claims data to understand SUA magnitude and geographic distribution.

Methods: The following variables were mapped: CDC Behavioral Risk Factor Surveillance System age-adjusted asthma mortality (2015) and self-reported prevalence (2014); Asthma and Allergy Foundation of America (AAFA) *Asthma Capitals* (2015)—reflecting a composite of prevalence, risk, medical factors determining cities with greatest disease burden; and QuintilesIMS anonymous patient-level prescriptions (4/2014–5/2017) and physician-affiliations data. Prescription-based morbidity (PBM) was defined as ICS/LABA prescriptions and ≥ 2 OCS prescriptions/year. States were ranked by percentage ICS/LABA asthmatics with PBM. Cities/counties with > 25 asthmatics prescribed ICS/LABA (7918) were included (county score weighted equally by number of ICS/LABA asthmatics and percentage PBM).

Results: US mortality/prevalence rates were 10.3/million and 7.6%, respectively. WV–12.5(mortality)/11% (prevalence), NY–13.1/10.7%, OH–12.3/10.7% were top-10 states for both mortality and prevalence. OH (7 *Asthma Capitals*), NY (5) were also top-10 for *Asthma Capitals*. However, CA (10), FL (9), TX (7) had as many, if not more, AAFA high-disease burden cities. 25% of 2,216,252 asthmatics with ICS/LABA prescriptions had ≥ 2 OCS bursts/year (17% of those on low-dosage ICS/LABA, 25% medium, 31% high). Although not top-10 mortality/prevalence states, FL, TN (4 *Asthma Capitals*), SC (3 *Asthma Capitals*) were top-10 for *Asthma Capitals* and PBM. Four FL counties (6 cities), 3 TN counties (4 cities), 3 SC counties (3 cities) met PBM criteria; 6 of these 13 cities being *Asthma Capitals* (FL-1, TN-2, SC-3). City/country variation in PBM was greater than state variation (SD 8% vs 4%). Five southern (GA, FL, SC, AL, TN), 2 midwestern (OH, PA) states had ≥ 3 PBM counties, despite 38 states having greater prevalence. Although not top-10 in mortality, prevalence, or *Asthma Capitals*, GA had the most PBM counties (9)/cities (12). Only WV was top-10 for prevalence (11%), mortality (12.5%), and PBM (2 counties/2 cities).

Conclusions: Findings indicate significant asthma morbidity heterogeneity across the US not reflected in individual state statistics. Disproportionate OCS use despite appropriate maintenance therapy occurs in counties/cities with and without state statistics reflecting SUA. State morbidity indices do not directly reflect locales with OCS overuse. Improved SUA awareness in areas with disproportionate OCS use and deploying regionally-directed education/clinical practice interventions could improve morbidity through appropriate use of therapies including targeted biologics.

Funded by: AstraZeneca

Insights into the Treatment and Progression of Pediatric Asthma

Miguel J. Lanz, MD; Ileen Gilbert, MD; Stanley J. Szeffler, MD; Kevin R. Murphy, MD

Introduction: Recent studies have suggested that poorly controlled asthma in childhood may lead to fixed airflow obstruction in adulthood. Unfortunately, there is a paucity of data regarding the progression of the disease, so clinicians are not entirely able to predict the course of a child's asthma. The present study assessed the current understanding of childhood asthma treatment and progression, as well as some remaining gaps in knowledge.

Methods: A nonsystematic PubMed literature search was performed. Articles were selected based on the authors' clinical experience and included discussions on the treatment of childhood asthma and prediction of progression into adulthood.

Results: Uncontrolled asthma in early childhood can adversely affect lung development, but it is not yet known if timely interventions such as inhaled corticosteroids (ICS) can preserve lung function in children through to adulthood. Recent studies have shown an ICS combined with a long-acting β_2 -agonist (LABA) is effective in children aged 6-12 years. Asthma phenotypes have recently been identified that can help predict which children may respond to a particular treatment. Targeted biologic therapies have shown promise in treating adults with severe, uncontrolled asthma, and some are approved in the United States for children as young as age 6 with particular phenotypes.

Conclusions: Children's asthma control and pulmonary function should be monitored over time in order to minimize any impact on lung development. Further studies are necessary to describe the factors contributing to lung function decline in children with asthma, as well as management strategies that could prevent or reverse this decline in pulmonary function.

Funding: AstraZeneca

Use of Oral Immunotherapy for Peanut Allergy and Current Management in US Patients

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Introduction: Peanut allergy is a major United States (US) health burden. Treatment is limited to avoidance and acute reaction management. No drug or medical product has been approved for use as a peanut oral immunotherapy (POIT) agent.

Methods: We conducted qualitative, in-depth, telephonic interviews with 28 community and academic allergists and 6 nurse food-allergy specialists across the US between April and June 2016. Interviewed clinicians managed >100 peanut allergy patients/year. For perspectives on POIT, we ensured that 50% of the allergists interviewed offered POIT in clinical studies or self-developed protocols.

Results: Conventional peanut allergy management is consistent across the US; patients are diagnosed via clinical history assessment, skin and/or blood tests; food challenges to confirm diagnosis are conducted in ~5-10% of patients. Protocols for non-standardized and unapproved OIT vary substantially. Areas of divergence include:

- **Patient selection:** Clinical history, risk of accidental exposure, and patient/family motivation and accountability levels are considered to varying extents
- **Peanut material:** Mostly store-bought products (whole peanuts, peanut flour, peanut butter); pharmacy compounded products rarely used
- **Starting dose:** 1mcg to 0.1mg whole peanut
- **End-dose:** 250mg to 5g whole peanut
- **Up-dosing interval:** Biweekly; a minority of protocols up-dose weekly

Among physicians not offering POIT, major barriers include medical-legal implications and lack of a proven and FDA-approved therapy.

Conclusions: Currently, substantial variability in approaches to POIT exists within the US. Several practices do not offer POIT and others use protocols not recommended in guidelines for peanut allergy. All physicians suggest a need for effective, FDA-approved, disease-modifying treatments.

Funding by: Aimmune

Wide Variability in Terminology Used in Oral Immunotherapy: Late-Breaking Results from a Diverse Sample of US-Based Allergists and Immunologists

Bradley E. Chipps; Christina E. Ciaccio; Karin Rosén; Tmirah Haselkorn; Thomas B. Casale

Introduction: The terminology used in food oral immunotherapy (OIT) varies globally. Given promising phase 3 results, OIT may soon become first-line treatment for peanut allergy, and a standard lexicon is needed. Real-world data were collected from diverse United States (US) allergists/immunologists to assess their preferred OIT terminology, especially when communicating with patients.

Methods: An online, self-administered survey was fielded to US allergists and/or immunologists between December 28, 2017 and January 27, 2018. Eligible participants completed training ≥ 5 years ago, spent >20% of their time in direct patient care, and managed ≥ 50 patients with food allergy.

Results: Of 101 total participants from 28 US cities, 78% spent 81-100% of their time in direct patient care and 48% had administered OIT in the past year. Respondents gave varying definitions for "reactive dose" during oral food challenge (OFC) as follows: "dose at which symptoms occur" (63%); "lowest dose at which symptoms occur" (14%); and "cumulative dose at which symptoms occur" (10%). Respondents' definitions of "tolerated dose" during OFC similarly varied: "highest dose tolerated without symptoms" (32%); "dose at which no symptoms occur" (30%); and "cumulative dose tolerated without symptoms" (11%). After OIT, 81% of participants identified "tolerated dose" as the most clinically meaningful for patients to understand; 88% felt that a stronger consensus on OIT terminology would be extremely or very useful.

Conclusions: OIT terminology varies considerably and a standardized lexicon is important for successful implementation, patient education, and safety. "Tolerated dose" was considered by physicians to be most clinically relevant for patients.

Funded by: Aimmune

Efficacy and Safety of AR101 in Peanut Allergy: Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial (PALISADE)

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Introduction: Peanut allergy is characterized by a high unmet medical need for treatments that reduce risks of peanut-allergic reactions following accidental exposures. AR101 is a novel oral immunotherapy (OIT) designed to address this unmet need.

Methods: PALISADE, the largest reported study of a treatment for peanut allergy, was an international, multicenter, randomized, double-blind, placebo-controlled phase 3 trial of AR101 OIT in peanut-allergic subjects aged 4-55 years. Eligible subjects reacted at ≤ 100 mg of peanut protein during double-blind, placebo-controlled food challenge (DBPCFC) at screening. Subjects completed initial escalation and up-dosing, ~6 months of 300 mg/day maintenance, and an exit DBPCFC. The primary analysis, reported here, included subjects aged 4-17 years.

Results: Of 750 screened primary analysis subjects, 496 were randomized (AR101 n=372, placebo n=124) and received ≥ 1 treatment dose. Among randomized subjects, 358 (72%) had a history of peanut anaphylaxis and baseline median (range) maximum tolerated peanut dose was 10 mg (3, 30 mg); 412 (83%) subjects completed PALISADE (296 [80%] AR101 and 116 [94%] placebo). Percentages of primary analysis subjects tolerating highest exit DBPCFC doses of 300, 600 (primary endpoint), and 1000 mg were 77%, 67%, and 50% for AR101, versus 8%, 4%, and 2% placebo, respectively (overall between-group difference: 63.2% [$P < 0.00001$]; 95% confidence interval: 53.0, 73.3). No deaths or life-threatening adverse events (AEs) occurred; among AR101 subjects, discontinuations occurred in 6.7% for gastrointestinal AEs and 2.7% following hypersensitivity reactions.

Conclusions: These data suggest AR101 is an effective treatment in reducing clinical reactivity to peanut in highly sensitized peanut-allergic patients.

Funded by: Aimmune

Characterization of pediatric onset common variable immunodeficiency (CVID) in a large cohort

Baloh CH, Reddy A, Buckley R & Lugar PL

Background: CVID is the most common treatable primary immune deficiency in children and adults. Current literature has yielded mixed results in characterizing pediatric onset CVID. No studies have fully explored mortality risk factors in pediatric onset CVID. This leaves limited data to guide pediatricians as they diagnose and follow patients with this disease.

Methods: Retrospective chart review of 204 subjects with CVID at a single institution, of whom 91 had disease onset at a pediatric age. Clinical and laboratory data were collected. Odds ratios and Fisher tests were utilized to examine trends. This study was IRB approved.

Results: The clinical features and laboratory results for subjects with pediatric onset CVID are similar to those who had adult onset CVID. However, the majority of the deceased subjects (13/18) were at a pediatric age at CVID symptom onset. These subjects had a lower age at mortality, multiple comorbidities, and often depression. The most common cause of death was infection. Lung disease (OR 5, $p < 0.05$) and infection with severe/opportunistic organisms (OR 9, $p < 0.05$) are directly related to increased mortality. Delay in diagnosis of CVID is also correlated with mortality. Intermediary markers correlating with mortality include anemia, GERD, and depression.

Conclusions: There are many similarities between pediatric and adult onset CVID, however, the mortality of pediatric CVID in our cohort is striking. This is the first study to identify specific factors correlated with mortality in pediatric onset CVID to guide pediatricians and subspecialists in managing these immune deficient patients.

SLE Treatment: Immunosuppressive Therapy A New Area

Marianne Frieri, M.D, Ph.D.

Background: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease, with many cytokines, autoantibodies produced against all body tissues and organs. Increased knowledge and research studies on the immunopathology of SLE has led to identification of multiple new immunotherapeutic agents targeting immune cells and cytokines.

Methods: Based on the literature review, recently most physicians use mycophenolate mofetil for induction therapy in mild to moderate proliferative lupus nephritis and cyclophosphamide in severe cases, and usually save rituximab for cases with frequent relapses or resistance. There are new studies which proves gradually stopping the immunosuppressant therapy can reduce flare ups.

There are several randomized clinical trials on the comparison of high dose vs. low dose cyclophosphamide plus azathioprine therapy for maintaining the response after both treatments, which recommend no significant differences between the two groups in most of them.

Discussion: The classic treatment for SLE in the past decades were methotrexate, azathioprine and/ or corticosteroids. The new area of SLE treatment started with immunotherapy in the last decade with one of the first successful treatments such as cyclophosphamide and followed by other important medications such as rituximab, azathioprine, mycophenolate and others.

Conclusion: There is an excitement about the new area of treatments with hopes for steady remissions that are getting higher with physicians to use the immunosuppressive agents more frequently. We should also consider the limitations on these new agents such as lack of long-term follow up, cytopenia, failure to have complete response in some patients, infection, and less commonly malignancy.

Rapid Onset of Action and Improvement of Nasal and Ocular Symptoms with Olopatadine/Mometasone Combination Nasal Spray in Patients With Seasonal Allergic Rhinitis

Niran J. Amar, Craig F. LaForce, Aurora Breazna, Cynthia F. Caracta, Sudeesh K. Tantry

Objective: In two randomized double-blind studies, twice-daily GSP301 nasal spray—a fixed-dose combination of olopatadine hydrochloride and mometasone furoate—significantly improved reflective total nasal symptom score (rTNSS) versus placebo (primary endpoint; presented elsewhere). GSP301 onset of action and reflective total ocular symptom scores (rTOSS) are presented here.

Methods: In each study (study 1 [NCT02631551]; study 2 [NCT02870205]), patients ≥ 12 years with Seasonal Allergic Rhinitis (SAR) were equally randomized to GSP301 (olopatadine 665 μg /mometasone 25 μg BID), olopatadine (665 μg BID), mometasone (25 μg BID), or placebo for 14 days. GSP301 onset of action was assessed by mean change from baseline in average instantaneous TNSS (iTNSS) at various timepoints (from 15 minutes to 4 hours post-dose) versus placebo and analyzed via mixed-effect model repeated measures, adjusting for covariates.

Results: A total of 1,180 and 1,176 patients were randomized in studies 1 and 2, respectively. A rapid onset of action for GSP301 was observed at 15 minutes post-dose versus placebo in study 1 (least squares mean difference [95% CI]: -0.35 [-0.63, -0.07]; $P=0.014$) and study 2 (-0.34 [-0.65, -0.04]; $P=0.028$), an effect that was maintained at each subsequent timepoint. Additionally, GSP301 statistically significantly improved rTOSS versus placebo (study 1: -0.49 [-0.79, -0.19], $P=0.0014$; study 2: -0.52 [-0.84, -0.20], $P=0.001$). Treatment-emergent adverse events were low and comparable across treatments.

Conclusions: In two SAR studies, GSP301 BID treatment had a rapid onset of action of 15 minutes, provided statistically significant improvements in ocular symptoms versus placebo, and was well tolerated.

Funding by: Glenmark Specialty SA

Efficacy and Safety of Olopatadine/Mometasone Combination Nasal Spray for the Treatment of Seasonal Allergic Rhinitis

Gary Gross, Frank Hampel, Aurora Breazna, Cynthia F. Caracta, Sudeesh K. Tantry

Objective: Combining an intranasal antihistamine with an intranasal corticosteroid for the treatment of allergic rhinitis (AR) may provide improved symptom relief over treatment with either drug alone. GSP301 nasal spray (NS) is a fixed-dose combination of the antihistamine olopatadine hydrochloride and the corticosteroid mometasone furoate. Efficacy and safety of GSP301 were evaluated in this Seasonal AR (SAR) study.

Methods: In this randomized, double-blind, parallel-group study, eligible patients (≥ 12 years) with SAR were randomized 1:1:1:1 to GSP301 (olopatadine 665 μg /mometasone 25 μg BID), olopatadine (665 μg BID), mometasone (25 μg BID), or placebo for 14 days of treatment. The primary endpoint—mean change from baseline in AM and PM reflective total nasal symptom score (rTNSS)—was analyzed via mixed-effect model repeated measures (MMRM). Adverse events (AEs) were also assessed.

Results: A total of 1,176 patients were randomized. GSP301 BID treatment statistically significantly improved rTNSS scores versus placebo (least square means difference [95% CI]: -1.09 [-1.49, -0.69]; $P < 0.001$). GSP301 BID treatment also showed significant improvement versus olopatadine (-0.44 [-0.84, -0.05]; $P=0.028$) and mometasone (-0.47 [-0.86, -0.08]; $P=0.019$). Olopatadine and mometasone monotherapies significantly improved rTNSS scores versus placebo (olopatadine: -0.64 [-1.04, -0.25]; $P=0.001$; mometasone: -0.62 [-1.01, -0.22]; $P=0.002$). Treatment-emergent AEs were reported by 15.6%, 12.6%, 9.6% and 9.5% of patients in the GSP301, olopatadine, mometasone, and placebo groups, respectively.

Conclusions: In this study, GSP301 BID treatment provided statistically significant and clinically meaningful improvements in SAR symptoms versus placebo and versus individual monotherapies. GSP301 BID treatment was well tolerated.

Funding by: Glenmark Specialty SA

Comparative Cost Analysis of Monitoring Exhaled Nitric Oxide (FeNO) in Asthma Management

Marc Massanari, PharmD , Andrew Layton , and Renee Arnold, Pharm.D;

Rationale: Asthma guidelines recommend periodic assessment and management of symptoms to prevent exacerbations, which can lead to hospitalization, increased healthcare utilization and cost. According to recent Cochrane meta-analysis data, FeNO monitoring is associated with a 40-50% reduction in the risk of exacerbations. Cost modelling of these data indicated the potential for significant cost savings with FeNO use. Therefore, we attempted to verify this potential for cost savings within a real-world database of Medicare recipients.

Methods: This retrospective observational study investigated asthma related claims from a Medicare database. Patients were included that had 2 years of records following an asthma-related inpatient hospitalization (IP) or emergency department (ED) claim and had a history of an asthma related event in the prior year. A case-crossover analysis was completed of asthma-related IP/ED events before and after FeNO use during the two year study period.

Results: 63 patients of 2,828 asthma patients who met the inclusion criteria had FeNO measured during the two-year study period. During the period before FeNO use, 61/63 (97%) patients had an asthma-related IP/ED event compared to 30/63 (48%) during the FeNO period. Asthma-related IP/ED claims and charges per patient per day during the period before FeNO were 0.026 and \$12,368 compared to 0.003 and \$1,340 during the FeNO period ($p < 0.018/0.0043$), respectively.

Conclusions: FeNO monitoring in patients with a history of exacerbations was associated with a substantial reduction in asthma related IP/ED claims and charges. These data support cost modelling estimates and demonstrates FeNO use in asthma management is cost-effective.

Funded by: Circassia

Assessment of Airway Inflammation Using Exhaled Nitric Oxide in Pediatric Asthma and Its Impact on Treatment Decisions

M Massanari, SJ Szeffler and BE Chipps

Rationale: Accurate diagnosis and management of asthma in children is challenging. Exhaled nitric oxide (FeNO) is an accurate biomarker of T2/type 2 airway inflammation and is used clinically to aid in the diagnosis of asthma, optimize steroid dosing, assess adherence and identify patients at risk for asthma exacerbations (Cochrane 2016, Hoch 2017).

Objective: Explore the real-world impact of measuring FeNO on treatment decisions among pediatric asthma specialists

Methods: Pediatric asthma specialists who had not used FeNO previously in their practice were invited to participate in the NIOX Experience Program. Before measurement of FeNO, physicians recorded baseline symptoms and medication use and assessed the likelihood of significant airway inflammation. FeNO was then measured and based on the result, physicians recorded necessary medication changes.

Results: Data were collected from 149 pediatric asthma specialists to investigate the impact of FeNO measurement in 1,237 pediatric patients <12 years old. 44% (544/1,237) of these patients were symptomatic upon presentation. 62% of patients were receiving an asthma controller medication. Clinical assessment of airway inflammation correlated with the measured FeNO in 70% (463/659) of patients when FeNO was low (<20ppb) compared to only 31% of patients (99/321) when FeNO was high (>35ppb). Presence or absence of symptoms influenced correlation of airway inflammation assessment; in asymptomatic patients a low likelihood of inflammation correlated with low FeNO in 64% (318/494) compared to symptomatic patients with a high likelihood and high FeNO in 59% (62/105). Changes in treatment based on the patient's FeNO were made in 39% of patients (481/1237); more frequently when FeNO was high in 77% (248/321) compared to low FeNO in 17% (114/659). Based on the high FeNO, ICS was increased in 25% (80/321), started in 41% (130/321) and oral steroid therapy started in 7% (22/321).

Conclusions: Recognition of airway inflammation was improved by measuring FeNO compared to clinical assessment in children. Knowledge of FeNO resulted in changes in asthma treatment. Specifically, when physicians became aware of high FeNO, anti-inflammatory treatment was increased.

Funded by: Circassia

Long-term Treatment Experience With Subcutaneous C1-Esterase Inhibitor for the Prevention of HAE Attacks: 2-Year Efficacy Results From the US COMPACT Open-label Extension Study

H. Henry Li, MD, Henrike Feuersenger, PhD, Joseph Chiao, MD, Thomas Machnig, MD, Iris Jacobs, MD, on behalf of the COMPACT Investigators

Introduction: Subcutaneous C1-esterase inhibitor (C1-INH [SC]) 60 IU/kg is indicated for routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adolescents and adults. Patients fulfilling the inclusion criteria of the phase III COMPACT study were eligible for enrollment into a long-term, open-label extension (OLE) study. We evaluated the efficacy of C1-INH (SC) in patients who used the approved dosage for >2 years.

Methods: COMPACT enrolled patients with HAE who had ≥ 4 attacks over 2 consecutive months. Patients from the United States who completed the 1-year treatment period of the OLE study could continue treatment for up to 88 additional weeks; efficacy was assessed at 6-month intervals.

Results: In the OLE study, 126 patients were randomized to receive C1-INH (SC) 40 or 60 IU/kg twice weekly; 110 completed the study. Of the 24 patients on 60 IU/kg who entered the extension period, 23 (12 M/11 F; mean age, 41 ± 15 years) continued treatment beyond 2 years for 1.5 to >6 months (overall duration of exposure, 2.3 ± 0.3 years). Prior to screening, the mean attack rate was 3.1 attacks/month. After 2 years of treatment, 83% of patients (19/23) were completely free of HAE attacks and symptoms between month 25 and 30; 87% (20/23) no longer used rescue medication. C1-INH (SC) was well tolerated and had a safety profile consistent with that observed in the COMPACT trial.

Conclusions: Long-term replacement therapy with twice-weekly C1-INH (SC) 60 IU/kg has a sustained and profound preventive effect in patients with HAE, with >80% of patients achieving symptom-free status.

Funded by: CSL Behring

Preva Long-term Experience With Subcutaneous C1-Esterase Inhibitor Prophylactic Therapy for Hereditary Angioedema: Case Reports From an Open-label Extension Study

Donald S. Levy, MD, John Anderson, MD, Joseph Chiao, MD

Introduction: Subcutaneous C1-esterase inhibitor (C1-INH [SC]) is indicated as routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adolescents and adults. Patients completing the pivotal phase III COMPACT study were eligible to enroll in a long-term, open-label extension (OLE) study. Patients completing 1 year of the OLE study could continue treatment for up to 88 additional weeks. We report on the experience of 2 patients treated with C1-INH (SC) for >2 years.

Methods/Case Presentations: Patient 1, a 43-year-old woman, and Patient 2, a 45-year-old man, were treated with C1-INH (SC) 60 IU/kg twice weekly for 16 weeks followed by low-volume placebo in the COMPACT study. Patients 1 and 2 continued treatment with C1-INH (SC) in the OLE study for 139 and 125 weeks, respectively.

Results: In the placebo-controlled study, the monthly attack rate decreased from 5.4 with placebo to 0.6 with C1-INH (SC) for Patient 1 and from 5.8 to 0.3 for Patient 2. Patient 1 had 1.2 attacks/month during the OLE period compared with 3.0 attacks/month before the study. Patient 2 experienced 3.7 attacks/month before the study but was nearly attack-free (0.1 attacks/month) over a 125-week period in the OLE study. In both patients, rescue medication use, number of HAE symptom days, and average attack severity also decreased during prophylaxis compared with the placebo periods. Both patients experienced improvements in quality-of-life measures.

Conclusion: Long-term prophylaxis with C1-INH (SC) can lead to sustained reductions in attack frequency and severity, improving quality of life in patients with HAE.

Funded by: CSL Behring

Safety Profile Of 300IR 5-Grass Tablet In Children With Grass Pollen-Induced Allergic Rhinoconjunctivitis In a Post-Marketing Safety Study

D. Golden, K. Staten, L. Beveridge, B. Geng

Introduction: We report safety data of 300IR 5-grass pollen tablet* from a post-marketing study conducted in grass pollen-allergic children in Europe.

Methods: This multicenter, observational study (NCT02295969) included allergy immunotherapy-naïve 5-9-year-old children with grass pollen-induced allergic rhinitis (AR) with/without conjunctivitis prescribed with 300IR tablet daily (3-day dose escalation). Patients whose parent/legal guardian provided written consent were followed for safety and tolerability during the first 30 treatment days. Adverse reactions (ADRs) were analyzed descriptively.

Results: 307 children entered the study. 70% were polysensitized, 76% had conjunctivitis, 36% had asthma. 173/307 patients (56%) reported ADRs, most frequently application-site reactions (e.g., throat irritation, oral pruritus, oral paresthesia). 73% of ADRs were mild, 24% moderate, 3% severe. ADRs occurred on Day 1 in 35% of patients reporting ADRs, Day 2: 25%, Day 3–Day 10: 60%, Day 11–Day 30: 49%. Regardless of onset day, ADRs occurred within the first 30 minutes after intake in 88% of patients. 16/307 patients (5.2%) discontinued due to ADRs (application-site reactions in 7 patients). Two patients reported serious reactions. One experienced oral pruritus, mild urticaria and asthmatic attack (grade II anaphylaxis, Day 5), received oral antihistamine/inhaled salbutamol and resumed treatment. One was hospitalized overnight for severe lip/eye swelling (angioedema, Day 26) resolved within six hours with IV antihistamine/corticosteroid. No epinephrine use nor ICU was reported.

Conclusion: The safety profile of 300IR tablet in children was consistent with that in patients older than 10 years, most ADRs being local and generally mild to moderate.

*Indicated in US in patients 10-65.

Funded by: Stallergenes Greer

House Dust Mite Allergic Subject Exposure And Immunological Response to 300IR House Dust Mite Sublingual Tablets In Four Phase III Trials

Y. Okamoto, M. Okano, K. Staten, L. Beveridge, M. Jutel

Introduction: We present subject exposure and results of immunological markers (IgE, IgG₄) in subjects with HDM-associated allergic rhinitis (HDM-AR) treated with 300IR HDM sublingual tablets (STG320)* in four Phase III trials. Results with 500IR were presented elsewhere.

Methods: Four DBPC trials: Trial-1 in adults (18-50 years; Europe; NCT00674700), Trial-2 in adults/adolescents (12-64 years; Japan; JapicCTI-121917), Trial-3 (5-17 years; Europe; NCT01199133) and Trial-4 (5-16 years; Japan; JapicCTI-152981) both in children/adolescents, enrolled subjects with medically confirmed HDM-AR for ≥ 1 or ≥ 2 years. Participants were randomized to HDM tablets (300IR or 500IR in Trials 1, 2; 300IR in Trials 3, 4) or placebo once daily (with dose-escalation) for one year. HDM-specific IgE and IgG₄ were assessed before and after treatment. End of treatment/baseline (EOT/BL) ratios were calculated (descriptive analysis).

Results: 2,386 subjects entered Trial-1 (N=509), Trial-2 (N=968), Trial-3 (N=471) or Trial-4 (N=438). Of them, 952 subjects received the 300IR tablet (Trial-1=170, Trial-2=322, Trial-3=241, Trial-4=219). In all trials, HDM-specific IgE increased in the 300IR groups (EOT/BL: 1.2-1.9) and remained stable in placebo groups (EOT/BL: 0.8-1.1) over treatment. HDM-specific IgG₄ were 2-fold higher or more in the 300IR groups (EOT/BL: 2.2-4.4) and little changed in placebo groups (EOT/BL: 0.9-1.6). In Trial-1 post-treatment year, IgE and IgG₄ remained higher in the 300IR group (EOT/BL: 1.2-3.3) compared to placebo.

Conclusions: Immunological data in 2,386 subjects from four Phase III trials support HDM sublingual tablets are immunologically active in HDM-AR subjects over treatment and remained so over the Trial-1 post-treatment year.

*STG320 is not approved in the US

Funded by: Stallergenes Greer

EDS-FLU (Exhalation delivery system with fluticasone) improves sleep in patients with nasal polyposis (NP)

Ellen R. Sher, MD; John C. Messina, PharmD; Jennifer L. Carothers, ScD, MBA; Per G. Djupesland, MD, PhD; Ramy A. Mahmoud, MD, MPH

Introduction: Patients with NP have poor sleep quality and worse quality of life scores and comorbid depression. EDS-FLU delivers intranasal steroid to superior/posterior sites, high and deep in the nasal passages where sinus ostia normally drain/ventilate and chronic inflammation occurs. This analysis examines the effect of EDS-FLU on sleep.

Methods: Sleep was assessed with the 7 sub-scales of the MOS Sleep-R scale and the sleep sub-scale of the Sinonasal Outcome Test (SNOT-22) in a randomized, 24-week (16 double-blind+8 open-label), placebo-controlled study. The Patient Global Impression of Change (PGIC) was also assessed. Subjects (N=323, mean age= 45.0, prior steroids=86.7%, prior surgery=30%) with moderate-severe symptoms and bilateral nasal polyps received EDS-FLU 93, 186 or 372mcg or EDS-placebo BID. Results for 186- and 372- μ g BID doses, which are recommended in FDA-approved product labeling, are presented.

Results: Improvements in the Sleep Problems Index were observed with EDS-FLU (LS mean change, Week 16: -15.8 and -14.3 with 186mcg and 372mcg, respectively versus -10.0 with EDS-placebo ($P \leq 0.038$)). Changes in other MOS-Sleep-R subscales, (sleep disturbance/snoring/shortness of breath or headache/adequacy/somnolence) also favored EDS-FLU. Changes on the SNOT-22 Sleep Function subscale at week 16 were consistent with the MOS-Sleep sub scales (LS mean changes: -3.04, and -3.14 with EDS-FLU 186mcg and 372mcg, respectively, versus -1.37 with placebo ($P \leq 0.001$)). Two-thirds of subjects in the active treatment arms reported being "much" or "very much" improved as assessed by PGIC versus 29% with placebo.

Conclusions: In patients with nasal polyposis, EDS-FLU treatment significantly improved various aspects of sleep. The overall treatment benefit was clinically meaningful.

Funded by: Optinose

Systemic Exposure to Fluticasone Propionate (FP) with an Intranasal Exhalation Delivery System with Fluticasone (EDS-FLU) 186 µg Versus Observed, Dose-normalized and Reported Orally-Inhaled Flovent® HFA 220 µg

Harry J. Sacks, MD; John C. Messina, PharmD; Jennifer L. Carothers, ScD, MBA; Elliot Offman, BPharm, PhD; Ramy A. Mahmoud, MD, MPH

Introduction: EDS-FLU delivers fluticasone propionate (FP) high and deep in the nasal cavity with less loss to drip-out and swallowing than conventional nasal sprays, resulting in increased intranasal on-target exposure. We evaluated if increased on-target exposure increases systemic exposure to FP compared to an approved FP product by comparing exposure from EDS-FLU and Flovent® HFA.

Methods: FP pharmacokinetic (PK) data was obtained following single doses of EDS-FLU 186µg and 372µg in healthy subjects (n=90) in Part A of a randomized, crossover study. In Part B, EDS-FLU 372µg and Flovent 440µg single-dose PK data were obtained in patients with mild-to-moderate asthma (n=27). A population PK model was fit to the EDS-FLU data to allow simulation of EDS-FLU 186µg under repeat-dosing conditions for comparison to the repeated-dose exposure reported for Flovent 220µg.

Results: Single doses of EDS-FLU 186µg produced lower FP C_{max} (16.03 vs. 19.89 pg/mL, geometric mean ratio [GMR]=80.6%) and substantially lower FP AUC_{0-∞} (100.50 vs. 200.05 hr-pg/mL, GMR=50.2%) in healthy subjects compared to single doses of Flovent 220µg (dose-normalized from 440µg) in mild-to-moderate asthmatics. Population PK data for repeat-dose AUC₀₋₁₂ and C_{max} following EDS-FLU 186µg BID was much lower than the steady-state exposure reported for Flovent 220µg BID (C_{max} 22.71 versus 45.8-80.6 pg/ml, GMR=28.2-49.6%; AUC₀₋₁₂ 123.8 versus 191.0-463.6 hr-pg/mL, GMR=26.7-64.8%).

Conclusions: EDS-FLU 186µg produces much lower systemic FP exposure than Flovent 220µg following single doses. Population PK exposure estimates for EDS-FLU 186µg BID at steady state show FP exposures that are low and below orally inhaled FP exposures previously proven to be safe.

Funded by: Optinose

EDS-FLU Improves Quality of Life and Health Status: Pooled Analysis of Phase 3 Trials Navigate I and II

Fulton F. Velez, MD; Harry J. Sacks, MD; John C. Messina, Jr, PharmD; Sam Colman; Ramy A. Mahmoud, MD, MPH

Introduction: Chronic rhinosinusitis (CRS) seriously impairs health related quality of life (HRQoL). Trials in CRS patients showed that EDS-FLU produced robust improvements in CRS symptoms, polyp grade, and surgical eligibility. This analysis describes the impact of EDS-FLU on individual domains of the 36-Item Short-Form Health Survey version 2 (SF-36v2), and on utilities, assessed via the Short-Form Six-Dimension (SF-6D).

Methods: Pooled randomized clinical trial data (NAVIGATE I and II; N5641) were analyzed to examine SF-36v2 and SF-6D change from baseline to end-of-double-blind (EODB: 16 weeks) and end-of-study (EOS: 24 weeks; 8 weeks open-label treatment). The SF-36v2 was scored using 2009 U.S. population norms (50 5 general population t-score); the SF-6D was calculated from UK population non-parametric preference weights.

Results: Mean baseline SF-36v2 scores were below population norms across treatment arms. At EODB, mean improvement was significantly greater for all SF-36v2 domain/summary scores with EDS-FLU (range: 2.9/physical functioning to 5.11/bodily pain) vs. EDS-placebo (range: 0.81/mental health to 2.87/bodily pain) (each comparison P<0.01). Similarly, SF-6D scores were significantly improved vs. placebo (0.058 vs. 0.023; P<0.001). Nine out of ten mean EODB domain/summary scores were at or above population norms for EDS-FLU vs. 4 out of 10 for placebo. At EOS, SF-36v2 and SF-6D scores improved in all treatment arms; all scored at or above SF-36v2 population norms.

Conclusions: In this pooled analysis of two large pivotal EDS-FLU trials, health domain and health utilities improvements were ~2-3 times greater with EDS-FLU than EDS-placebo after 16 weeks. End-of-study improvements were at or above population norms for all treatment arms.

Funded by: Optinose

Real world experience with eds-flu (exhalation delivery system with fluticasone propionate) from the patient's perspective: A follow-up patient survey

Maeva O'Connor, MD; Fulton Velez, MD; John McGinnis, MPH; Harry Sacks, MD

Introduction: Patients with chronic rhinosinusitis with or without nasal polyps (CRSw/sNP) report suboptimal symptom control and frustration with current treatments. EDS-FLU (XHANCE™) is a new approach to intranasal delivery of a topical steroid. In clinical trials, it improved multiple symptoms, eliminated nasal polyps in some patients, and decreased surgical eligibility. The product recently became available and early treatment satisfaction and preference for EDS-FLU were assessed.

Methods: Participants in a special access program (Xperience) who received EDS-FLU were offered the opportunity to complete a phone survey to receive their first prescription refill at no-cost to them. Assessment questions included adherence, previous intranasal steroid (INS) use, symptoms change, ease of use, satisfaction, preference vs. INS and whether they would recommend EDS-FLU. Results are for responders during the first two months of the program.

Results: At cutoff, 321 patients completed the survey; 64% had used conventional INS and 10% used budesonide irrigations (within 6 months). Among responders, 81% reported symptom improvement, 87% treatment satisfaction, 81% preferred EDS-FLU to prior INS, and 89% stated they would recommend EDS-FLU. Recent fluticasone users (N=80) reported symptom improvement/satisfaction/preference/recommend levels with EDS-FLU of 83%/85%/90%/89%, while recent budesonide irrigation users (N=33) reported 79%/97%/91%/94%. Spontaneously-reported adverse events were consistent with those reported in clinical trials. Limitations include generalizability of early adopters and responder bias.

Conclusions: In this real-world experience survey among patients recently starting EDS-FLU, most patients reported improved symptoms, treatment satisfaction, and EDS-FLU preference for EDS-FLU compared to previous nasal steroids. EDS-FLU may be an important new option for patients who receive INS.

Funded by Optinose

Efficacy of switching human plasma-derived C1 esterase inhibitor to recombinant human C1 esterase inhibitor as prophylaxis in a patient with type 1 hereditary angioedema

John Anderson, MD, Angela Haynes, PharmD; E. Trey CaJacob, BS; Diane Paige, BSN, CCRC

Introduction: Recombinant human C1 esterase inhibitor (rhC1-INH) is indicated for acute hereditary angioedema (HAE) attacks in adolescents/adults. Trial data have also shown rhC1-INH to be efficacious as prophylaxis. We report the efficacy of switching prophylactic therapy from human plasma-derived C1-INH (pdC1-INH) to investigational rhC1-INH.

Case Report: A 29-year-old African-American male was diagnosed with type I HAE at age 19 years and received pdC1-INH prophylaxis 1000 IU every 3-4 days, which was increased several times up to 2500 IU every 3-4 days because of HAE attack frequency. Despite prophylaxis, he experienced an average of 2-3 attacks per week and rated pdC1-INH effectiveness as a "6" (range, 1-10; 10 being "extremely effective"). During ~9 years of pdC1-INH prophylaxis, his treatment was interrupted several times because of medication supply shortages. The dose and dosing schedule were adjusted to attempt to overcome these disruptions, but the adjustments contributed to an increase in HAE attack frequency. Due to a recent shortage, the patient was switched from pdC1-INH to rhC1-INH therapy (4200 IU approximately every 2 days). During 6 months of rhC1-INH prophylaxis, the patient has stabilized, with no adjustments in dosing or frequency required. He rated the effectiveness of rhC1-INH therapy in preventing HAE attacks an "8" and has reported fewer breakthrough attacks. Unlike with pdC1-INH therapy, the patient has had no treatment interruptions with rhC1-INH and is not concerned about potential treatment disruptions because of medication shortages.

Conclusion: Switching patients from pdC1-INH to rhC1-INH prophylaxis can be effective in patients with HAE.

Funded by: Pharming

Recombinant human C1-esterase inhibitor for the prevention of acute hereditary angioedema attacks: A case report

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Purpose: Prophylaxis may be considered for frequent acute attacks of hereditary angioedema (HAE); moreover, prophylaxis efficacy may impact direct costs associated with medical utilization/medication. This case report presents the efficacy and cost savings of investigational prophylactic treatment with recombinant human C1 esterase inhibitor (rhC1-INH).

Case Report: A white female aged 52 years who had experienced HAE attack symptoms since age 16 years was diagnosed at age 37 years with type 1 HAE. She received danazol 400 mg/d; attempts to lower dose were unsuccessful. She continued to experience daily extremity swelling and had abdominal edema with intense pain severe enough to warrant hospitalization every 2-3 months. In 2012, she began prophylaxis with plasma-derived C1-INH (pdC1-INH) 1000 IU 3 times weekly (TIW) at a weekly cost of ~\$16,500. During a 12-month period (September 2013 to September 2014), the authors documented 13 emergency room (ER) visits for an acute HAE attack, but other records suggest there were several additional ER visits. The pdC1-INH dose was increased to 1500 IU TIW in October 2014 at a weekly cost of ~\$24,829, and the number of ER visits declined (n=9 during a 14-month period). In December 2015, the patient began prophylaxis TIW with rhC1-INH 2100 IU for an annual cost savings of \$400,660 versus pdC1-INH. From initiation of rhC1-INH to October 2017, the patient required only 1 ER visit.

Conclusion: rhC1-INH prophylaxis for HAE reduced the occurrence of ER visits and provided a potential cost benefit in terms of both drug costs and medical utilization.

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Efficacy of recombinant human C1 esterase inhibitor as prophylaxis for hereditary angioedema attacks in a patient tolerant to other therapies

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Purpose: Studies have shown that recombinant human C1 esterase inhibitor (rhC1-INH) may prevent acute attacks of hereditary angioedema (HAE). Here, we report the long-term efficacy of investigational prophylactic rhC1-INH in a patient with severe HAE who became refractory to human plasma-derived C1-INH (pdC1-INH) prophylaxis.

Case Report: A 20-year old white female was diagnosed with type 3 HAE (normal plasma C1-INH concentrations) at age 15 years and experienced multiple HAE attacks per week despite prophylactic treatment with pdC1-INH 1500 IU twice weekly. Over the course of approximately 1.5 years, she experienced an average of 2 moderate HAE attacks per week while receiving pdC1-INH prophylaxis. She then began to have daily acute attacks. The dose of pdC1-INH was increased to 2000 IU twice weekly and then increased again to 2500 IU twice weekly with no effect on attack severity and frequency. Due to insufficient response, the patient was switched to investigational prophylactic treatment with rhC1-INH 6300 IU twice weekly and experienced improved efficacy in preventing HAE attacks. The patient currently receives rhC1-INH 4200 IU three times weekly and experiences <1 HAE attack per week. Since beginning rhC1-INH, the patient has experienced a mean of 2.5 attacks per month (ie, ~30 acute HAE attacks per year), with no indication of tolerance during 3 years of rhC1-INH prophylaxis.

Conclusion: rhC1-INH prophylaxis substantially reduced the occurrence of acute HAE attacks in a patient refractory to pdC1-INH therapy.

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Healthcare Resource Utilization due to Chronic Urticaria in Europe, South America, and Central America: Findings From Visit 1 of the Worldwide AWARE Study

Marcus Maurer, Luis Felipe C. Ensina, Gérard Guillet, Katherine F. Houghton, Ismail Kasujee

Introduction: Chronic urticaria (CU) is characterized by repeated occurrence of itchy hives and/or angioedema for ≥ 6 weeks. We assessed real-world healthcare resource utilization (HRU) of patients with CU in Europe and Central/South America (C/SA) in the AWARE study.

Methods: Patients were aged ≥ 18 years and refractory to ≥ 1 course of H₁-antihistamine. Medical visits due to CU were assessed and Work Productivity and Activity Impairment (WPAI) questionnaire scores collected. Descriptive statistics are reported for data collected at enrollment (Visit 1).

Results: Of 4,226 patients (Europe: n=3,733; C/SA: n=493), 63% were employed (Europe: 63%; C/SA: 59%). C/SA patients were more likely to visit dermatologists/allergists (51% vs 47%) and less likely to visit general physicians (32% vs 57%) than European patients. Emergency room visits due to CU were more common in C/SA (40%; mean [SD] number of visits per patient, 23.2 [124.3]) than Europe (29%; 3.7 [11.4]). Hospital admissions due to CU were more common in Europe (22%) than C/SA (8%), but mean (SD) number of admissions among those hospitalized was greater in C/SA (3.3 [4.7] vs 2.0 [3.1]). Mean (SD) overall WPAI scores were 7.0 (18.9), 25.1 (26.8), 27.3 (28.5), and 33.3 (30.8) for absenteeism, presenteeism, work productivity loss, and activity impairment, respectively; C/SA patients reported higher rates of impairment (13%–36%) vs European patients.

Conclusions: CU is associated with substantial HRU, and work and activity impairment. General physicians should be considered key members of the treatment team in the care of these patients in Europe and C/SA.

Funded by: Novartis

AWARE-AMAC: First Baseline Characteristic Data From a Large Non-interventional Study on the Management and Clinical Impact of Chronic Idiopathic/Spontaneous Urticaria in Patients Refractory to H₁-antihistamines in Asia, Middle East and Africa

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Introduction: Chronic urticaria (CU) is characterized by the repeated occurrence of wheals and/or angioedema for ≥ 6 weeks. We describe real-life clinical outcomes, treatment patterns, resource utilization, and quality of life in patients with chronic idiopathic/spontaneous urticaria (CIU/CSU) and/or chronic inducible urticaria in countries from the Asia, Middle East, and Africa (AMAC) region.

Methods: Observational, prospective study in 15 countries of patients aged ≥ 18 years with CU refractory to H₁-antihistamines. Baseline characteristics are summarized by descriptive statistics.

Results: Baseline data are available for 908 patients: mean (SD) age, 39.8 (13.3) years; 69.7% female; 53.4% Caucasian, 38.0% Asian. Of 414 patients reporting angioedema, 36.7% had angioedema at baseline (35.5% mild, 46.1% moderate, 18.4% severe). At baseline, in patients with/without angioedema: mean (SD) duration of CIU/CSU, 27.0 (44.9)/29.9 (52.4) months; mean (SD) Urticaria Activity Score, 2.9 (1.7)/2.8 (1.7); mean (SD) Physician Global Assessment of disease control visual score (0: no control, 100: complete control), 46.4 (29.3)/50.7 (27.5) mm; mean (95% CI) Dermatology Life Quality Index score, 12.0 (11.3, 12.7)/10.2 (9.6, 10.8). 34.3%/41.5% with/without angioedema were managed with H₁-antihistamines only. Cyclosporine, omalizumab, and montelukast, alone or in combination with H₁-antihistamines, were administered, respectively, to 1.0%, 27.8%, 3.4%/0.8%, 17.4%, 2.6% of patients with/without angioedema. 33.1%/36.6% of patients with/without angioedema received other classes of treatment or combinations of cyclosporine, omalizumab, or montelukast.

Conclusions: In this large real-life study, CIU/CSU characteristics at baseline confirmed the severity of the disease and the need for adequate treatment in patients in Asia, Middle East, and Africa.

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Chronic Inducible Urticaria (CIndU) in Europe, Central America, and South America: Findings From Visit 1 of the Worldwide AWARE Study

Marcus Maurer, Luis Felipe C. Ensina, Gérard Guillet, Katherine F. Houghton, Ismail Kasujee

Introduction: Chronic inducible urticaria (CIndU) is characterized by itchy wheals and/or angioedema. The real-world rate of CIndU in Europe (EU) and Central/South America (C/SA) is unknown. We examined diagnosis, disease control (measured by Urticaria Control Test [UCT]), and quality of life (QoL; measured by Dermatology Life Quality Index) in patients with CIndU in EU and C/SA in the AWARE study.

Methods: Patients were aged ≥ 18 years and refractory to ≥ 1 course of H₁-antihistamine. Data were collected at enrolment (Visit 1). Descriptive statistics are reported for the overall population and by region.

Results: Overall, 26% (n=1,118) of patients with chronic urticaria were diagnosed with CIndU: 31% had angioedema (current or within past 6 months); 77% had CIndU comorbid to chronic idiopathic/spontaneous urticaria (CIU/CSU). The rate of CIndU was higher in C/SA vs EU (33% vs 26%), but rates of angioedema and CIndU comorbid to CIU/CSU were similar. Rates of light/solar, vibratory, aquagenic, and contact urticaria were low (0.7%–6.2%). C/SA patients had a higher rate of symptomatic dermographism (53% vs 44%) and delayed pressure urticaria (30% vs 25%) but a lower rate of cold urticaria (10% vs 18%) and cholinergic urticaria (8% vs 18%) vs EU patients. UCT scores identified poor disease control in 77% of patients with CIndU (C/SA, 84% vs EU, 76%). Patients reported moderate (25%), very large (26%), or extremely large effect (7%) of CIndU on QoL.

Conclusions: CIndU is commonly associated with CIU/CSU, is uncontrolled in most patients, and can be severely disabling.

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Crisaborole Ointment Improves Global Atopic Dermatitis Severity Across Patients With Varying Baseline Characteristics: Pooled Results From Two Phase 3 Trials

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Introduction: Crisaborole ointment is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild to moderate atopic dermatitis (AD). Efficacy and safety of crisaborole for treatment of patients ≥ 2 years old with mild to moderate AD stratified by baseline characteristics was assessed in a post hoc analysis of 2 Phase 3 studies (NCT02118766; NCT02118792).

Methods: Crisaborole:vehicle (2:1 ratio) was administered twice daily for 28 days. Primary endpoint was success in Investigator's Static Global Assessment (ISGA), defined as scoring clear (0) or almost clear (1), with ≥ 2 -grade improvement from baseline at day 29. Efficacy and safety were stratified by age group (2 to <7 [n=506], 7 to <12 [n=436], 12 to <18 [n=371], and ≥ 18 years [n=209]), sex, use of prior AD treatment, disease severity (mild or moderate), and percentage affected body surface area (%BSA; 5% to <16% [mild], ≥ 16 % [moderate to severe]).

Results: The proportion of crisaborole-treated patients with success in ISGA vs vehicle-treated patients was 30.5% vs 21.8% (2 to <7 years; $P=0.0644$), 36.6% vs 22.9% (7 to <12 years; $P=0.0037$), 30.3% vs 19.4% (12 to <18 years; $P=0.0257$), 29.7% vs 24.7% (≥ 18 years; $P=0.4622$), 24.9% vs 21.2% (mild disease; $P=0.3470$), and 36.7% vs 22.3% (moderate disease; $P<0.0001$). Efficacy results in other subgroups were similar. Rate of application site pain ranged from 2.3% to 7.0% in crisaborole-treated patients across subgroups.

Conclusions: Pooled analysis from 2 Phase 3 trials showed that crisaborole improved global disease severity across multiple baseline characteristic subgroups.

Funded by: Pfizer

Efficacy and Safety of Crisaborole Ointment, 2%, for Treatment of Mild to Moderate Atopic Dermatitis (AD) Across Racial and Ethnic Groups

Valerie D. Callender, Andrew F. Alexis, Linda F. Stein Gold, Mark Lebwohl, Huaming Tan, William C. Ports, Anna M. Tallman

Introduction: Crisaborole ointment is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild to moderate AD. In 2 identically designed Phase 3 trials of patients with mild to moderate AD, crisaborole was superior to vehicle for the primary endpoint, success in global disease severity (pooled, crisaborole vs vehicle: 32.1% vs 21.8%, $P<0.001$). Incidence of treatment-related, treatment-emergent adverse events (TEAEs) was low. Pooled, post hoc analysis assessed efficacy and safety of crisaborole per race and ethnicity.

Methods: Patients received crisaborole or vehicle twice daily for 28 days. Primary endpoint was a score of clear (0) or almost clear (1), with a ≥ 2 -grade improvement from baseline at day 29 in Investigator's Static Global Assessment (ISGA). Safety included TEAEs. Post hoc analysis was by race (Asian, black, white, and other [American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, other]) and ethnicity (Hispanic/Latino [HL] or not Hispanic/Latino [nHL]).

Results: More crisaborole-treated patients than vehicle-treated patients had success in ISGA at day 29 (crisaborole vs vehicle): Asian: 20.6% vs 14.2%; black: 32.1% vs 24.6%; white: 33.5% vs 22.3%; other: 29.1% vs 13.2%; HL: 35.4% vs 18.2%; nHL: 31.3% vs 22.8%. Treatment-related TEAEs were (crisaborole vs vehicle) Asian: 5.1% vs 5.7%; black: 6.7% vs 2.2%; white: 7.2% vs 6.3%; other: 16.4% vs 4.0%; HL: 8.5% vs 8.1%; nHL: 7.1% vs 4.3%. The most frequent was application site pain.

Conclusions: Regardless of race or ethnicity, crisaborole reduced global disease severity in patients with mild to moderate AD, with a low frequency of treatment-related TEAEs.

Funded by: Pfizer

Long-Term Safety of Crisaborole Ointment, 2%, Across Racial and Ethnic Groups With Mild to Moderate Atopic Dermatitis (AD)

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Introduction: Crisaborole ointment is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild to moderate AD. A post hoc analysis assessed long-term safety of crisaborole by race and ethnicity.

Methods: Patients aged ≥ 2 years who completed 1 of the Phase 3 pivotal studies (NCT02118766, NCT02118792) without experiencing safety issues were enrolled in a 48-week, open-label safety study. Assessed for AD severity every 4 weeks, patients received 4 weeks of crisaborole if AD severity was at least mild by Investigator's Static Global Assessment. Treatment-emergent adverse events (TEAEs) had onset on or after treatment initiation in the Phase 3 studies. Post hoc analysis was by race (Asian, black, white, and other [other/American Indian/Alaskan Native]) and ethnicity (Hispanic/Latino [HL] or Not Hispanic/Latino [nHL]).

Results: 517 patients were enrolled: Asian: 5.6%; black: 29.4%; white: 60.9%; other: 4.1%; HL: 15.9%; nHL: 84.1%; percentage of patients reporting ≥ 1 TEAE: Asian: 51.7%; black: 50.0%; white: 72.1%; other: 85.7%; HL: 69.5%; nHL: 64.1%; percentage of patients reporting treatment-related TEAEs: Asian: 10.3%; black: 7.9%; white: 10.5%; other: 23.8%; HL: 14.6%; nHL: 9.4%. TEAEs resulting in discontinuation of crisaborole treatment were application site dermatitis (black: 1; nHL: 1), application site pain (white: 1; other: 1; nHL: 2), dermatitis atopic (black: 2; white: 3; HL: 3; nHL: 2), and eczema (white: 1; nHL: 1).

Conclusions: The rates of treatment-related TEAEs and discontinuations owing to TEAEs were similar in all groups except the other group. This should be interpreted with caution because of the small sample size of the other group.

Funded by: Pfizer