Eastern Allergy Conference
May 28 – 31, 2015 ~ Palm Beach, FL

All Scientific Posters will be on display in the South Ballroom Foyer, beginning Friday morning, May 29th. Authors of these posters are requested to be at their poster to discuss their work from 10:00 – 10:45 am, both Friday and Saturday.

Not for CME Credit

High Chinese Elm Pollen counts in the Fall in Atlanta, Georgia: 2009-2013

Shams M., Fineman S.

RATIONALE- Hayfever symptoms directly correlate with atmospheric pollen concentrations. Climatic and environmental factors have the ability to influence local botany and aerobiology. National Allergy Bureau pollen count stations determine the presence of local, clinically relevant allergens and track patterns of prevalence. This data is extremely valuable to treating allergists as knowledge regarding yearly and seasonal fluctuations in pollen counts is important in the managing patients with allergic rhino-conjunctivitis, in order to provide appropriate treatment regimens.

METHODS- Atmospheric sampling for aeroallergens in Atlanta, GA was preformed over a nine-year interval according to National Allergy Bureau standards using Rotorod sampler. Samples were collected each morning by trained observers and various pollens are counted. Atmospheric concentrations are determined by calculation from the raw counts. The pollen counting station was moved a distance of 2.2 miles in 2010. The staff is certified through the American Academy of Allergy, Asthma and Immunology Aeroallergen Network.

RESULTS- The southeast has an intense spring pollen season with very high tree pollen counts. Late summer-fall pollen season in past years is less intense and characterized by a ragweed bloom. However, through 2009-2013, there were very high levels of Chinese Elm during August and September. The pollen counts were consistently within the moderate range as determined by NAB criteria as greater than 15 grains per cubic meter. Peak counts ranged between 39.1- 475.2 grains/cubic meter and 4-day average ranged between 23.5-206.2 grains/cubic meter. Notable, was the increasing duration of the season and days spent within the moderate pollen range.

CONCLUSIONS- Chinese Elm has not been a dominant local aeroallergen in Atlanta, Georgia. It appears that due to a variety of climatic and environmental factors over the last several years, the prevalence of Chinese Elm pollen in metro-Atlanta has increased. The change of positioning of the pollen collection device may also be a factor for these extremely high counts, nevertheless Chinese Elm is an important aeroallergen and should be considered in patients having predominant summer-fall symptoms, especially if they fail to respond to Ragweed testing or immunotherapy which presents during the same time of year.

Targeting passive prophylaxis: Gender and breastfeeding determine susceptibility for severe respiratory syncytial virus (RSV) infection and protective efficacy of palivizumab in very low birth weight infants in a developing country

E.Kathryn Miller, Romina Libster, Tatyana Plachco, Lucrecia Bossi, Gabriela Bauer, Jodell Jackson, Norma Aspres, Fernando P. Polack

Background: Passive prophylaxis with humanized monoclonal antibody against RSV (palivizumab®) is recommended during the respiratory season to prevent severe illness in some. Exploration of subpopulations of premature infants with differential susceptibility for RSV has been limited.

Methods: We are conducting an ecological study in two High Risk Clinics caring for very low birth weight (VLBW) infants in Buenos Aires, Argentina. Two cohorts of 119 and 78 VLBW infants were followed prospectively until a corrected gestational age of 12 months between 2003-2005 and 2011-2013. Palivizumab® became available for VLBW infants in the Clinics in 2007. We aimed to assess the effectiveness of palivizumab® in the population and to explore comparative effectiveness in breastfed and nonbreastfed infants stratified by sex.

Results: Demographic and clinical comparisons between the cohorts revealed no major differences. Interestingly, 50% vs. 30% non-breastfed females were hospitalized pre and post-palivizumab® due to all ARI. No differences in admission rates were observed in breastfeeding females and males, and non-breastfeeding males. RSV caused 10% of hospitalizations between 2003-2005 and 5% between 2011-2013. Despite limited power for analysis, non-breastfed infants seemed to benefit from palivizumab® prevention against RSV hospitalizations: in females, 25% vs. 5% and in males, 15% vs. 5% hospitalizations were observed.

Conclusions: In this early assessment, the overall impact of palivizumab® prophylaxis was most evident in nonbreastfed VLBW females, decreasing hospitalizations due to all ARI by 40% based on an 80% decrease in admissions due to RSV. A rational and targeted administration of prophylactic treatment against RSV may enable protection of particularly vulnerable subpopulations.

In Vitro Characterization of Flunisolide HFA Particle Size and Particle Distribution

Alexander D'Addio, PhD; John Karafilidis, PharmD; Eli Meltzer, MD

Purpose: The objective of these in vitro experiments was to determine the aerodynamic particle size distribution (APSD) of flunisolide HFA (80 µg/actuation) with built-in spacer (Aerospan) compared to fluticasone propionate (Flovent, 110 µg/actuation) with a valved holding chamber (F/VHC) and without VHC (F) and beclomethasone (QVAR, 40 µg and 80 µg/actuation) with a valved holding chamber (Q/VHC, 80 µg only) and without VHC (Q for 40 and 80 µg).

Methods: Determination of APSD was performed using NGI (Next Generation Impactor) test set-up for metered dose inhalers (MDIs) as described in USP /Ph.Eur. Mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD), fine particle mass (FPM [≤5.0 µm][µg/shot]), dose delivered to impactor, fine particle fraction (FPF [% dose to impactor]), and fine particle fraction (FPF [%ND]) were calculated for each measurement. Percent nominal dose (%ND) was calculated as measured dose to impactor/claimed nominal dose.

Results: The flunisolide HFA mean MMAD was 1.2 ± 0.1 µm. The F/VHC and F MMADs were 2.3 ± 0.1 µm and 2.6 ± 0.1 µm, respectively. The Q/VHC and Q MMADs were 0.9 ± 0.1 µm and 1.0 ± 0.1 µm, respectively for 80 µg and 0.9 ± 0.0 µm for the 40 µg dose without the holding chamber. FPM was highest (77 µg ± 2 µg) with flunisolide HFA compared to F/VHC (57 ± 9 µg) and F (50 ± 1 µg). The FPF with flunisolide HFA (92.6%) was comparable to F/VHC (87.3%) and nearly twice that of F (46.5%). The FPF [%ND] with flunisolide HFA (96.9%) was approximately twice that with both F/VHC (51.5%) and F (45.1%) and greater than Q/VHC (80 µg only - 81.4%) and Q (80 µg - 70.2%; 40 µg - 70.4%).

Conclusions: The FPF with flunisolide HFA was greater than fluticasone and beclomethasone with and without a chamber. The dose to impactor was consistent with the labeled claim for the product. These results suggest that the built-in spacer within Aerospan is as effective as VHC (in terms of FPF) and superior to all devices tested without VHC.

Supported by Meda

Efficacy of Dymista Nasal Spray in the Treatment of Nasal Congestion in Patients with Seasonal Allergic Rhinitis (SAR)

Ellen Sher, MD, William E. Berger, MD, John Karafilidis, PharmD

Purpose: The objective of this analysis was to evaluate the efficacy of MP-AzeFlu, a single intranasal formulation of azelastine HCL (AZE) and fluticasone propionate (FP) for the treatment of nasal congestion in patients with SAR.

Methods: This evaluation included four, 2-week, double-blind, placebo- and active-controlled studies (studies 4001, 4002, 4004, and 4006). A total of 3999 patients were included in the Intent-to-Treat (ITT) population. MP-AzeFlu was compared to monotherapy with AZE and FP and all treatment were compared to placebo. Treatments were administered 1 spray per nostril twice daily (AM and PM). Total daily doses of AZE and FP were 548 mcg and 200 mcg, respectively. The primary efficacy variable was change from baseline in the 12-hour reflective total nasal symptom score (rTNSS), which included nasal congestion, sneezing, itchy nose, and runny nose scored twice daily (AM and PM) on a 4-point rating scale such that the maximum daily score was 24.

Results: MP-AzeFlu was statistically superior ($P<.05$) to placebo and to each monotherapy for improving rTNSS in all the studies. MP-AzeFlu was statistically superior to placebo in each of the studies for improving nasal congestion. Significant differences favoring MP-AzeFlu for improving nasal congestion were seen vs. AZE in all studies and vs. FP in studies 4001 and 4004. MP-AzeFlu was well tolerated. The most frequently reported adverse events with MP-AzeFlu were dysgeusia (4%), epistaxis (2%), and headache (2%).

Conclusions: Results of these studies demonstrate that MP-AzeFlu provided statistically significant improvement in nasal congestion compared to monotherapy with either AZE or FP.

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Randomized Trial of the Safety of Dymista Nasal Spray Compared with Fluticasone Propionate Nasal Spray in Children Ages ≥4 years to <12 years Years with Allergic Rhinitis

Ellen Sher, MD, William Berger, MD, John Karafilidis, PharmD

Purpose: Azelastine hydrochloride with fluticasone propionate (FP) in a single nasal spray (Dymista, MP-AzeFlu) is approved for the treatment of patients 6 years of age and older with seasonal allergic rhinitis. The objective of this study was to evaluate the safety of MP-AzeFlu compared to fluticasone propionate (FP) nasal spray, administered as 1 spray per nostril twice daily in pediatric subjects ≥4 years to <12 years with allergic rhinitis (AR).

Methods: In this randomized, open-label, 3-month study, qualified subjects had a history of AR, were in good health, and had no evidence of nasal mucosal erosion, nasal ulceration, nasal septum perforation, or any significant nasal disease. Subjects were randomized in a 3:1 ratio to MP-AzeFlu (n=304) or FP (n=101). Safety was assessed by subject and/or caregiver-reported adverse events (AEs), nasal examinations, vital signs, and laboratory assessments.

Results: Overall, 94% of subjects treated with MP-AzeFlu and 92% treated with FP completed the study. The most frequently reported AEs with MP-AzeFlu and FP, respectively, were: epistaxis (10% and 9%), headache (7% and 3%), cough (4% and 3%) and pyrexia (3% and 2%). The discontinuation rate due to AEs was 2% with MP-AzeFlu and 4% with FP. Laboratory parameters showed no meaningful changes in either treatment group and the groups were comparable for mean changes in vital sign measurements. There were no findings of nasal mucosal ulceration or septal perforation.

Conclusions: MP-AzeFlu and FP were well-tolerated during this 3-month study when administered as 1 spray per nostril twice daily in pediatric subjects ≥4 years to <12 years with AR.

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Evaluation of Efficacy of Flunisolide HFA (AEROSPAN) in Children 4 to 11 Years of Age: A Sub-Group Efficacy Analysis by Baseline Asthma Medication Use

David Skoner, MD, Alex D'Addio, PhD, John Karafilidis, PharmD

Purpose: Flunisolide HFA is an inhaled corticosteroid for treatment of asthma in patients 6 years and older. Flunisolide HFA is delivered through a built-in spacer that reduces oropharyngeal deposition and achieves an extra-fine particle size. A 12-week, multicenter, placebo- and active-controlled trial in pediatric patients 4 to 11 years (n=513) with mild-to-moderate asthma was conducted, with 80 mcg and 160 mcg BID doses of flunisolide HFA compared to 250 mcg and 500 mcg BID doses of flunisolide CFC. Post-hoc analyses evaluated the effect of flunisolide HFA by baseline asthma medication, either an inhaled corticosteroid [ICS] or antileukotriene agents.

Methods: Sub-groups were analyzed for the primary endpoint (change from baseline to 12 weeks of treatment in % predicted FEV1). The most commonly used ICSs prior to study entry were: beclomethasone (n=129; mean daily dose of 236.7 mcg); fluticasone (n=69; mean daily dose of 325.3 mcg) and triamcinolone (n=52; mean daily dose of 445.5 mcg). Antileukotrines were montelukast and zafirlukast (n=38).

Results: Patients treated with flunisolide HFA, following a 2-week run-in with flunisolide CFC 500mcg BID, had % predicted FEV1 values that improved over their previous ICS. Respective mean improvements in % predicted FEV1 were: 7.6% (80 mcg) to 4.8% (160 mcg) for the beclomethasone subgroup; 2.9% (80 mcg) to 6.3% (160 mcg) for the fluticasone subgroup; and 13.6% (80 mcg) to 8.0% (160 mcg) for the triamcinolone subgroup. In addition, patients treated with antileukotrienes had a 7.7% (80 mcg) to 14.7% (160 mcg) improvement in % predicted FEV1.

Conclusions: After 12-weeks of treatment**,** pediatric patients 4 to 11 years treated with flunisolide HFA (80 and 160 mcg BID) had meaningful improvements in efficacy as assessed by % predicted FEV1, regardless of previous ICS.

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Variability of Repeat EggsIgE Levels

Tricia D Lee, MD, Manish Ramesh, MD, PhD, Jacob Kattan, MD, Julie Wang, MD

Rationale: Food specific IgE (sIgE) levels correlate with oral food challenge outcomes, however no guidelines exist regarding the interval to repeat testing. We examined the change for egg sIgE levels over time.

Methods: This retrospective chart review included all patients at our teaching institution who had egg sIgE drawn on 2 or more occasions and had a diagnosis code of food allergy (693.1), personal history of allergy to egg (V15.03), or anaphylaxis (995), between January 1, 2003, and November 1, 2012.

Results: 1077 patients had 2 or more egg sIgE levels performed. 206 (19.1%) patients , <2 years old (median age 1.26 years), had an initial sIgE ≥2 kU_A/L (95% predictive of clinical reactivity, median sIgE 15.10 kU_A/L), and 40 (19.4%) of these patients (median initial sIgE 4.23 kU_A/L) had any subsequent sIgE <2 kU_A/L, which all achieved by 5.54 years old. 394 (36.6%) patients , ≥2 years old (median age 4.87 years), had an initial sIgE ≥7 kU_A/L (median initial sIgE 21.7 kU_A/L). Of these patients, 97 (24.6%) patients had any subsequent sIgE <5 kU_A/L, and 13 (3.3%) patients (median initial age 4.57 years, median initial sIgE 11.1kU_A/L) had any subsequent sIgE level <2 kU_A/L, which all achieved by 10.56 years old.

Conclusions: Patients who have lower initial values and are younger are more likely to have a subsequent sIgE level <2 kU_A/L. Patients should have yearly egg sIgE levels until 11 years of age.

Patients with Rheumatologic Disorders May Develop Pain with Immunoglobulin Replacement, Requiring the Use of Daily Subcutaneous Therapy

Alan Koterba, MD PhD; Mark R. Stein, MD FAAAAI

Rationale: Intravenous immune globulin (IVIG) has been associated with systemic side effects including back and joint pain. Subcutaneous immune globulin (SCIG) has a lower incidence of systemic side effects including pain. Patients with existing rheumatologic disease may be at risk for joint pain following IVIG/SCIG infusion.

Methods: We present three cases of patients who had acute severe joint pain with IVIG or SCIG. Their dosing strategies were subsequently modified by administering daily SCIG.

Results: A 51 year old male with common variable immune deficiency and juvenile rheumatoid arthritis had back, joint pain and hypertension after his first dose of IVIG. One week later the pain was so disabling he was bedbound and unable to work. His SCIG regimen was changed to 2g 6days/week without pain, remaining infection free with stable IgG levels (850mgd/l).

A 51 year old male with CVID, CREST syndrome, and monoclonal gammopathy, developed severe muscle and generalized joint pain 3 days after his first dose of SCIG. His SCIG regimen was titrated from daily to 3g daily 3x/week which was well tolerated and IgG levels have remained stable in the 1000mg/dl range.

A 50 year old female with fibromyalgia and specific antibody deficiency reported worsening fibromyalgia pain which was relieved by changing to one gram daily SCIG.

Conclusions: This experience suggests a need for caution and pre-medication when starting certain patients with rheumatologic conditions on SCIG or IVIG. Daily SCIG dosing may be an alternative strategy for patients who are not able to tolerate standard dosing.

A Prospective, Open-Label Study of a New Albuterol Multidose Dry Powder Inhaler (MDPI) With Integrated Dose Counter

John Given, MD[1]; Herminia Taveras, PhD, MPH[2]; Harald Iverson, PhD[2]

Introduction: Albuterol MDPI, which includes an integrated dose counter and eliminates the need for coordination of inhalation with actuation, was evaluated.

Methods: This phase 3, prospective, open-label study (NCT01857323) enrolled patients (≥4 years) with asthma or chronic obstructive pulmonary disease who demonstrated adequate MDPI inhaler technique and ≥90% compliance with dosing and diary completion during run-in. Patients received twice-daily albuterol MDPI (2 inhalations/dose; 90mcg/inhalation) for ≤50 days. Patients reported discrepancies between albuterol MDPI counter readings and dose cycles in daily diaries. Primary endpoint: occurrence rate/200 dose cycles of "dose-cycle undercount" (counter display did not count down). Secondary endpoints: "dose-cycle overcount" (counter display decreased by >1), "count-unknown dose cycle" (display before dosing <the counter number; end of previous dose), "count-up-unknown dose cycle" (display before dosing >the counter number; end of previous dose), and total inhaler discrepancy size (total discrepancy for counter versus dose cycles). Ease-of-use/satisfaction (questionnaire; 7-point scale) and adverse events (AEs) were assessed.

Results: Overall rate of "dose-cycle undercount" discrepancies was 2.05/200 dose cycles. Mean (±standard error) estimated absolute value of total discrepancy size after 200 doses was 2.07±0.140. Estimated probability of exceeding absolute total discrepancy size of 10 dose cycles/200 dose cycles was low (0.0009). Most (83%) patients were somewhat/very satisfied and >90% were satisfied with device ease of use. No deaths and 2 serious AEs (atrial fibrillation/supraventricular tachycardia, n=1; skin eruption, n=1) occurred.

Conclusions: Albuterol MDPI with dose counter functioned reliably and accurately and was generally well tolerated with a high degree of patient satisfaction.

Supported by Teva Pharmaceuticals.

Dose-Ranging Study of a Fluticasone Propionate (Fp) Multidose Dry Powder Inhaler (MDPI) in Adolescents and Adults With Asthma Uncontrolled by Noncorticosteroid Asthma Medications

Edward M. Kerwin, MD; Michael Gillespie, MS; Sharon Song, PhD; Jonathan Steinfeld, MD

Introduction: A novel MDPI eliminates the need for coordination of actuation with inhalation. The efficacy, pharmacokinetics (PK), and safety of 4 different doses of Fp MDPI versus placebo MDPI and Fp dry powder inhaler (DPI) were evaluated.

Methods: This 12-week, double-blind, parallel-group, dose-ranging study (NCT01479621) randomized asthma patients (N=622) aged ≥12 years to twice-daily treatment with Fp MDPI (12.5, 25, 50, or 100mcg), placebo MDPI, or Fp DPI 100mcg. Primary efficacy endpoint was change from baseline over 12 weeks in trough (morning predose and pre-rescue bronchodilator) forced expiratory volume in 1 second (FEV_1). In the PK subpopulation (n=95), blood samples were collected pre-dose and at specified intervals post-dose on day 1. PK parameters included area under the plasma concentration-vs-time curve from time 0 to last measurable concentration, maximum observed concentration (C_{max}), and time of C_{max} (t_{max}). Adverse events were monitored.

Results: Change from baseline in trough FEV_1 over 12 weeks was significantly (P<0.01) higher versus placebo MDPI at Fp MDPI 25, 50, and 100mcg. There were no significant differences between FEV_1 change from baseline over 12 weeks for any Fp MDPI dose and Fp DPI 100mcg. C_{max} increased with increasing Fp MDPI doses and t_{max} was similar across doses and treatments. Systemic exposures for Fp MDPI 25 and 50mcg were lower than Fp DPI 100mcg, with similar benefits. Fp MDPI safety profile was similar to Fp DPI.

Conclusions: Changes in FEV_1 with Fp MDPI 25 and 50mcg were comparable to Fp DPI 100mcg, with lower systemic exposure.

Supported by Teva Pharmaceuticals.

A Novel Albuterol Multidose Dry Powder Inhaler (MDPI) in Adult and Adolescent Patients With Exercise-Induced Bronchoconstriction (EIB): A Single-Dose Study

Nancy K. Ostrom, MD, CPI; Herminia Taveras, PhD, MPH; Harald Iverson, PhD; David S. Pearlman, MD

Introduction: A novel, inhalation-driven MDPI eliminates the need to coordinate actuation with inhalation. We evaluated the efficacy and safety of albuterol (AB) MDPI for prevention of EIB.

Methods: This single-dose, double-blind, 2-way crossover study (NCT01791972) evaluated adolescents and adults with EIB (≥20% fall from pre-exercise challenge forced expiratory volume in 1 second [FEV_1]) randomized to 2 inhalations of AB MDPI 90mcg (total dose 180mcg)/placebo (PBO) MDPI (n=19) or the reverse sequence (n=19). FEV_1 was measured 30 and 5 minutes pre-dose and 30 minutes post-dose, 5 minutes before treadmill exercise challenge (baseline), and 5, 10, 15, 30, and 60 minutes post-exercise. Primary efficacy endpoint was maximum percentage FEV_1 fall from baseline up to 60 minutes post-exercise. Secondary efficacy endpoints included percentage of patients whose maximum percentage fall from baseline FEV_1 post-exercise was <10% (fully protected by treatment) and time to recovery (from exercise completion to first measured post-exercise FEV_1 within 10% of pre-exercise baseline FEV_1).

Results: Mean maximum percentage FEV_1 fall within 60 minutes post-exercise for AB MDPI was 6.21±1.44% (95% CI, 3.28%-9.14%) vs PBO, 22.38±1.44% (95% CI, 19.44%-25.31%; P<0.0001). Thirty-two (84.2%) AB MDPI patients had <10% maximum FEV_1 fall post-exercise vs 6 (15.8%) PBO patients (P<0.0001). Protection with AB MDPI was significant (P<0.0001) vs PBO 5 minutes post-exercise; recovery was complete for both groups at 60 minutes. No serious adverse events, discontinuations due to adverse events, or deaths occurred.

Conclusions: AB MDPI provided clinically significant protection from EIB in adolescents and adults with a history of EIB.

Supported by Teva Pharmaceuticals

Dose-Ranging Study to Evaluate the Efficacy and Safety of Four Doses of Fluticasone Propionate/Salmeterol Multidose Dry Powder Inhaler Compared With Fluticasone Propionate Multidose Dry Powder Inhaler and Fluticasone Propionate/Salmeterol Dry Powder Inhaler in Patients With Persistent Asthma

Jonathan Steinfeld, MD; Gloria Yiu, MS; S. David Miller, MD

Introduction: We conducted a dose-response efficacy/safety study of 4 single-dose regimens of fluticasone/salmeterol multidose dry powder inhaler (FS MDPI) versus fluticasone propionate (Fp) MDPI and FS dry powder inhaler (DPI) in patients with asthma.

Methods: This multicenter, randomized, double-blind, single-dose, 6-period crossover, dose-ranging study (NCT01772368) randomized patients (N=72; aged ≥12 years with persistent asthma and predose maximum forced expiratory volume in 1 second [FEV_1] 40%–85% of predicted normal) to FS MDPI 100/6.25mcg, 100/12.5mcg, 100/25mcg, or 100/50mcg; Fp MDPI 100mcg; or FS DPI 100/50mcg. Efficacy was evaluated by measuring baseline-adjusted FEV_1 area under the curve over 12 hours post-dose (AUC_{0-12}). Pharmacokinetics over 12 hours post-dose and tolerability were assessed.

Results: Baseline-adjusted FS MDPI 100/50mcg FEV_1 AUC_{0-12} was significantly higher than FS DPI (least-squares mean 57.88; P=0.0017). FS MDPI 100/25mcg trended toward higher efficacy (34.14; P=0.0624), FS MDPI 100/12.5mcg was comparable (3.42; P=0.8503), and FS MDPI 100/6.25mcg was significantly lower than FS DPI (−41.7 mL; P<0.0229). All doses of FS MDPI and FS DPI were significantly higher versus Fp MDPI (P<0.001). Pharmacokinetics demonstrated lower salmeterol AUC_{0-t} for FS MDPI 100/6.25mcg, 100/12.5mcg, and 100/25mcg versus FS DPI; AUC_{0-t} for FS MDPI 100/50mcg was higher. All FS MDPI doses were generally well tolerated.

Conclusions: Improvements in FEV_1 AUC_{0-12} were greater for all FS MDPI doses versus Fp MDPI at the same Fp dose, demonstrating the value of adding salmeterol to Fp MDPI for asthma treatment. FS MDPI 100/12.5mcg demonstrated similar bronchodilation to FS DPI 100/50mcg with lower systemic exposure to salmeterol.

Supported by Teva Pharmaceuticals.

Pharmacokinetics, Safety, and Tolerability of Fluticasone Propionate Multidose Dry Powder Inhaler and Fluticasone Dry Powder Inhaler Administered in Healthy Subjects: An Open-Label, Randomized, Three-Period Crossover, Single-Dose Study

Apinya Bee Vutikullird, DO; Michael Gillespie, MS; Sharon Song, PhD; Jonathan Steinfeld, MD

Introduction: Fluticasone (Fp), an inhaled corticosteroid with well-established safety and efficacy, is available as a dry powder inhaler (DPI) formulation and a hydrofluoroalkane inhalation aerosol. In this study, Fp was delivered via a novel, inhalation-driven multidose DPI (MDPI) that eliminates the need to coordinate actuation with inhalation.

Methods: This single-center, open-label, randomized, 3-period crossover, single-dose study randomized healthy Japanese and Caucasian subjects (N=30) to 1 of 6 treatment sequences including combinations of 4 inhalations of Fp MDPI 100mcg (total dose, 400mcg), Fp MDPI 200mcg (total dose, 800mcg), and Fp DPI 100mcg (total dose, 400mcg). Primary objective was pharmacokinetics (PK) assessment (maximum plasma concentration and time, terminal rate constant and half-life for plasma elimination, area under concentration-vs-time curve) for each treatment; safety and tolerability also were assessed.

Results: Over the range of Fp doses evaluated, PK parameters were similar in all subjects. Differences in systemic exposures were dose-dependent, with Fp plasma concentration-vs-time curves highest for Fp MDPI 800mcg and lowest for Fp DPI 400mcg. The most frequently occurring adverse event was presyncope (n=2 Caucasian subjects; 1 Fp MDPI 400mcg, 1 Fp MDPI 800mcg). There were no clinically significant treatment-related adverse events.

Conclusions: PK profiles for all doses were similar in Japanese and Caucasian subjects. Differences in systemic exposures were dose-dependent, with Fp MDPI 800mcg highest and Fp DPI 400mcg lowest. Safety and tolerability profiles of all treatments were consistent with the known profile of Fp.

Supported by Teva Pharmaceuticals.

Apps for Food allergy: A critical assessment

Cuervo-Pardo L, Barcena-Blanch MA, Gonzalez-Estrada A, and Schroer B

Introduction: There is currently no standardized control for accuracy or quality of recommendations/information in health-care related apps. We analyzed the most commonly available food allergy apps in order to identify applications that provide scientific and useful information for users.

Methods: We performed an online search in the Itunes app store using the keywords “food allergy” and “food allergens” from October 3-5, 2014. All apps for Apple IOs were included in the initial analysis but all dietary, gluten, and food additive directed apps were excluded. We analyzed app type (information, tool, or both), price, features, and content. A scoring system (0-100%) was created to assess multiple app features including quality and accuracy in food allergy information. A score equal or above 90% was considered accurate for health care information in food allergy. Three medical reviewers analyzed each app.

Results: A total of 79 food allergy apps were analyzed out of 191 available. Tool apps were the most common type of app (75.3%). The three most common tools included scanner (27.5%), food diary (23.5%), and symptom tracker apps (21.5%). The median app price was 99 cents. The most common feature was social media network support (43.6%). The median app score was 8% (mean 17.84, SD 21.81). Only two apps were considered accurate (≥90% score) for food allergy education.

Conclusion: Most available food allergy apps are a poor source of information for patients. This stresses the importance of in-office teaching and guidance regarding accurate social media tools for patient health-care information.

Comparativebeans and black gram: Evaluating the possibility of clinical cross or co-reactivity

Siddanakoppalu N. Pramod, Afua O. Tetteh, Richard E Goodman

Introduction: Taxonomically diverse legumes are consumed globally, but their allergenicity varies widely. Major seed storage proteins of legumes share high sequence identities and some are important allergens. But some are differentially glycosylated and previous studies demonstrate that plant glycans may act as irrelevant IgE binding targets. Our study intent was to differentiate protein epitopes from irrelevant glycan epitopes among subjects with common SPT and laboratory IgE binding.

Methods: Sera from individuals reporting food allergy to legumes were tested for specific IgE to legume extracts of soybean, navy bean and black gram using dot-blots, 1-D SDS-PAGE immunoblots and ELISA. IgE inhibition was performed with native extracts. The IgE binding proteins were identified by LC-MS/MS and full-length sequences aligned for identity comparison.

Results: Individual IgE binding patterns varied between subjects. However, eight sera with comparable levels of legume-specific IgE showed clear binding to proteins in soybean (20 kD), navy bean (45, 34 and 29 kD) and black gram (44 kD), which were identified as seed storage glycoproteins by LC-MS/MS. The relative intensity of IgE binding on immunoblots was similar results from ELISA. Inhibition dot blot and ELISA indicate possible cross-reactivity among these legumes and these proteins share sequence identity (50-70%).

Conclusions: In vitro IgE binding and inhibition indicate possible allergenic cross-reactivity among seed storage proteins of common beans and black gram among legume sensitized subjects. However, subtle differences were noted in the efficiency of IgE binding, inhibition demonstrating a need for further studies to define the IgE binding epitopes.

SELECTED PERINATAL OUTCOMES IN PREGNANT WOMEN EXPOSED TO OMLIZUMAB: INTERIM RESULTS FROM A PROSPECTIVE, OBSERVATIONAL STUDY

Jennifer Namazy, Abdelkader Rahmaoui, Michael D. Cabana, Angela E. Scheuerle, John M. Thorp, Jr., Gillis Carrigan, Elizabeth B. Andrews

Introduction: Data regarding maternal and fetal outcomes for many asthma medications are insufficient.

Methods: EXPECT is an ongoing prospective, observational study of pregnant women exposed to ≥1 dose of omalizumab within 8 weeks prior to conception or at any time during pregnancy. Data on mother and pregnancy/infant are collected at enrollment, each trimester of pregnancy, pregnancy outcome, and up to 18 months post-delivery. Maternal asthma severity is assessed by mother’s health provider. Data collected: rates of live births, spontaneous abortions, elective terminations, stillbirths, birth weight, gestational age, and congenital anomalies. Data are from an annual cumulative summary including September 29, 2006 -November 30, 2013.

Results: Of 207 prospectively enrolled pregnancies, outcomes from 186 pregnancies were reported. Asthma severity was available for 164 women: mild (4/164, 2.4%), moderate (55/164, 33.5%), severe (105/164, 64.0%). There were 174 live births of 178 infants (4 twin pairs), 8 spontaneous abortions, 2 fetal deaths/stillbirths and 2 elective terminations. Of 170 singleton infants, 24 (14.1%) were born prematurely (<37 weeks) and of these 3 (12.5%) were considered small for gestational age (SGA, $<10^{th}$ percentile). Of 140 singleton full-term infants with weight data, 4 (2.9%) had low birthweight and 16 (11.4%) were considered SGA. Overall, 27 infants had confirmed congenital anomalies (15.2%). Eleven infants had a major birth defect (6.2%); omalizumab exposure occurred in the first trimester in all cases. No pattern of anomalies was observed.

Conclusions: Given the small sample size and severity of maternal asthma, these pregnancy outcomes are not inconsistent with previous observations.

Supported by Genentech

Efficacy of omalizumab in allergic asthma by asthma severity and eosinophilic status

Nicola A. Hanania, Benjamin Trzaskoma, Karin Rosén, Volkan Manga, and Theodore A. Omachi

Introduction Response to biologic therapies for the treatment of asthma may be predicted by clinical and biologic markers of asthma severity.

Objectives This post-hoc analysis was conducted to determine if clinical markers of asthma severity and blood eosinophils predict response to omalizumab (OMA) treatment for severe allergic asthma.

Methods Data were pooled from 2 phase 3 pivotal trials of OMA in allergic asthma (N=1071). The number of asthma exacerbations requiring systemic corticosteroids was analyzed over the 16-week-inhaled corticosteroid-stable dose phase of the studies. Effects of OMA on exacerbations relative to peripheral blood eosinophil counts (<300/μL[low] vs ≥300/μL[high]), use of long-acting beta agonists (LABAs), and asthma hospitalization in the year prior to screening were examined.

Results Exacerbations were reduced 53% with OMA vs PBO (95% CI, 33–68; $P<0.001$) in those requiring systemic corticosteroids; 75% in patients receiving LABAs (95% CI 30-91; $P=0.008$) compared with 47% not receiving LABAs (95% CI, 23–65; $P=0.001$); and 63% (95% CI, 34–79; $P<0.001$) with higher blood eosinophils compared with 39% with lower eosinophils (95% CI, 0–63; $P=0.051$). In patients hospitalized for asthma in the year prior to screening, no exacerbations occurred in 17 OMA-treated patients vs 17 exacerbations in 31 PBO patients, for a 100% reduction ($P<0.001$). Exacerbations were reduced 42% in patients not requiring hospitalization in the prior year (95% CI, 14–60; $P=0.006$).

Conclusions Patients with greater asthma severity, as assessed by baseline LABA use, prior hospitalizations for asthma, or higher blood eosinophil counts, have a better response to OMA.

Supported by Genentech

Psoriasiform Spongiotic Dermatitis and Autoimmune Disease

Marianne Frieri, MD, PhD, Sisira Sran, MD, Marcelo Taborga, MD

Background: Inflammatory skin diseases manifest via reactive physiological pathways to pathogens. (1). Epidermal keratinocytes, which are highly active immunological cells, produce cytokines, chemokines, and express surface molecules, which play a major role in both the acute and chronic phases of skin inflammation (2). In acute eczematous dermatitis, activated dermis-infiltrating T cells secrete proinflammatory cytokines that may direct single epidermal keratinocytes to undergo either apoptosis or survival**.** TNFα may promote both keratinocyte apoptosis and limit the spread of keratinocyte damage, leading to the formation of spongiosis, the histopathological hallmark of acute eczematous dermatitis (3).

Case: A 76 year old female was referred to the allergy clinic with intermittent lesions in her left lower extremity. The patient had similar resolved lesions in her chest and upper extremity Her medical history is significant for rheumatoid arthritis, Sjogren's disease, fibromyalgia, breast cancer with bilateral mastectomy, gastroesophageal disease, myocardial infarction, neuropathy, depression, anxiety disorder, COPD/asthma, dyslipidemia and hypothyroidism. She was on numerous 23 medications for her conditions. Physical examination was significant for an ulcer in the left lower extremity near the ankle without any significant edema

Results: RF, CCP, B cell markers, CD19, CD29, CD23, CD10, surface immunoglobulin, myeloid, platelet and natural killer cell, stem cell, erythroid cell markers and NBT were within normal limits. Allergen testing by sIgE for birch, common ragweed, giant ragweed, timothy grass, shrimp, lobster, crab were normal. Immunoglobulin A and M and complement levels were normal. Immunoglobulin G levels were decreased at 573. A dermatopathology report of the left lateral anterior ankle revealed spongiosis, epidermal hyperplasia, and a superficial perivascular and interstitial mixed inflammatory cell infiltrate with lymphocytes, histiocytes and eosinophils.

Conclusion: Sjögren's syndrome is a systemic autoimmune disease characterized by the sicca complex,symptoms which includes dry oral mucosa, dry eyes, and arthritis (4).Skin findings in Sjögren's syndrome occur in half of the affected patients and may be unrecognized or undiagnosed, compared to the oral and ocular manifestations. There are few case reports of atopic dermatitis complicated by Sjögren's syndrome, however, like our patient, these patients presented with persistent itchy dry skin, eczematous lesions, and were affected by sicca symptoms (5). Perivascular infiltrates of lymphocytes, histiocytes, and occasional eosinophils, can occur in dyshydrotic eczema in rheumatoid arthritis, similar to the histopathology reported above (6). Drug eruptions may present with cutaneous inflammation including spongiotic, lichenoid, and psoriasiform dermatitis (7). In psoriasiform dermatitis, the microenvironment of interacting inflammatory cells, antigen presenting cells, and epithelial cells is disturbed, leading to stereotyped reaction patterns in inflammatory skin diseases. Proinflammatory cytokines play a role in the pathogenesis of rheumatoid arthritis as in spongiotic dermatitis.

An Itch for Berries: Blackberry-induced Urticaria

John Johnson D.O., Ali Saad D.O., Haig Tcheurekdjian M.D., Robert Hostoffer D.O.

INTRODUCTION: Allergic reactions to blackberries are exceedingly rare. However, allergic reactions due to other members of the Rosaceae family have been well published, especially in relation to birch pollinosis. We describe a case of a 39-year-old male with a convincing history and physical findings highly suggestive of blackberry-induced urticaria.

METHODS: IgE-mediated hypersensitivity to blackberry was evaluated using specific IgE serologies to black berry, skin prick testing to a variety of related berries, and oral food challenge to blackberry.

RESULTS: Skin prick testing strawberry did not demonstrate any cutaneous changes. IgE serologic testing was negative for blueberry, strawberry, raspberry, and blackberry. Subsequently, the patient's blackberry food challenge test was positive.

CONCLUSION: This is unique case of blackberry hypersensitivity confirmed by oral food challenge. **DISCUSSION:** As fresh fruits, including blackberries, become an increasing part of the American diet due to a variety of reasons, including fad diets and increasing produce availability, more patients will likely develop an allergy to blackberries. Even though this case demonstrated negative IgE serology, the oral food challenge test was positive, which is the gold standard for diagnosing food allergies. Further studies are needed to evaluate the role of food challenge testing patients with a clinical history suggestive of allergic reactions to blackberries in order to prevent future episodes of life-threatening anaphylaxis.

Omalizumab normalizes levels of high-affinity IgE receptor-positive skin cells in patients with chronic spontaneous urticaria (CSU): a randomized, double-blind, placebo-controlled study

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Introduction: The mechanism of action of omalizumab, a humanized recombinant monoclonal anti-IgE antibody, in CSU was explored, specifically effects on levels of high-affinity IgE receptor-positive (FcεRI+) and IgE-positive (IgE+) skin cells. Efficacy and pharmacokinetics/pharmacodynamics in CSU patients were assessed.

Methods: In a double-blind study, CSU patients aged 18–75 years were randomized to 300 mg omalizumab (n=20) or placebo (n=10) subcutaneous every 4 weeks for 12 weeks (doses: Days 1, 29, and 57). Lesional and non-lesional skin was biopsied at Days 1, 8, 29, 85 and 140. Biopsies from 10 untreated healthy volunteers (HVs) were a reference for histopathology data from treated patients. Efficacy was assessed using Weekly Urticaria Activity Scores (UAS7).

Results: The omalizumab group showed a significantly greater decrease in UAS7 than placebo at Day 85 (mean [SD] -23.1 [12.94] vs -8.1 [14.45]). CSU patients had higher FcεRI+ and IgE+ skin cell levels than HVs at Day 1. FcεRI+ cell levels in lesional and non-lesional skin declined significantly in omalizumab-treated patients. Decreases were seen by Day 29 in non-lesional skin, continuing to Day 85. IgE+ skin cell levels exhibited a non-statistically significant decline in omalizumab-treated patients (lesional: p=0.135; non-lesional: p=0.058). FcεRI+ and IgE+ cell levels in lesional and non-lesional skin in omalizumab-treated patients at Day 85 had declined to HV levels. The placebo group showed no meaningful change in FcεRI+ or IgE+ cells. Omalizumab pharmacokinetics/pharmacodynamics were consistent with previous studies.

Conclusion: Omalizumab is effective in CSU treatment, and decreases FcεRI+ cells in lesional and non-lesional skin to levels seen in healthy individuals.

Supported by Novartis and Genentech, Inc.

Angioedema and quality of life associated with chronic idiopathic/ spontaneous urticaria (CIU/CSU): subgroup analyses of two Phase III omalizumab trials in patients with recurrent angioedema despite H_1-antihistamine treatment

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Introduction: Angioedema, present in ~50% of CIU/CSU patients, negatively impacts health-related quality of life (QoL). We examined angioedema and Dermatology Life Quality Index (DLQI) scores of omalizumab-treated patients with baseline angioedema.

Methods: Data were pooled from ASTERIA I+II, 24-/12-week, placebo-controlled trials of omalizumab (75 mg, 150 mg and 300 mg every 4 weeks) in patients with CIU/CSU symptomatic despite approved H_1-antihistamine doses.

Results: Overall, 282/640 (44.1%) patients had baseline angioedema. Response to omalizumab was observed after the baseline injection; by Week 12, 60.8% (31/51), 65.5% (36/55) and 79.7% (47/59) of omalizumab 75 mg, 150 mg and 300 mg-treated patients, respectively, and 50.8% (31/61) of placebo patients were angioedema free. The mean number of angioedema days/week (standard deviation; SD) was reduced: baseline, 3.8 (2.1, n=66), 3.6 (2.1, n=76), 3.1 (2.0, n=66) and 3.0 (1.9, n=74), omalizumab 75 mg, 150 mg, 300 mg and placebo; Week 12, 1.3 (2.2, n=51), 1.1 (1.9, n=55), 0.5 (1.1, n=59) and 1.4 (1.8, n=61), respectively. The mean proportion of angioedema-free days from Weeks 4 to 12 was 79.0%, 80.7% and 90.7% with omalizumab 75 mg, 150 mg and 300 mg, respectively, vs placebo (78.6%; $p<0.0001$ vs 300 mg). The mean change from baseline to Week 12 (SD) on the DLQI was −7.0 (7.5, n=50), −8.0 (6.0, n=55), −12.9 (7.1, n=58), and −6.2 (7.1, n=60) with omalizumab 75 mg, 150 mg and 300 mg, and placebo, respectively.

Conclusion: Omalizumab may reduce the number of angioedema days in CIU/CSU, which may improve QoL.

Supported by Novartis and Genentech, Inc.

Dual Treatment Initiation With Timothy Grass and Ragweed Sublingual Immunotherapy Tablets is Well Tolerated in Adults with Allergic Rhinoconjunctivitis

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Introduction: Dual treatment with grass and ragweed sublingual immunotherapy tablets (SLIT-tablets) has not been studied. Safety and tolerability of dual treatment was assessed.

Methods: This open-label, multi-center trial enrolled North American adults (N=102) allergic to grass and ragweed. The trial had 3 periods, each of 2 weeks duration. In period 1, subjects received once-daily Timothy grass SLIT-tablet (2800 BAU; Merck/ALK). In period 2, subjects received short ragweed SLIT-tablet (12 Amb a 1-U; Merck/ALK) every morning and grass SLIT-tablet every evening. In period 3, subjects received both once-daily grass and ragweed SLIT-tablets within 5 minutes. The primary endpoint was the proportion of subjects with ≥1 local swelling events in each period. Secondary endpoints were the proportion of subjects with ≥1 local adverse events (AE), that discontinued due to AEs, and with ≥1 local AEs requiring treatment.

Results: No systemic allergic reactions, asthma attacks, or reactions requiring epinephrine were reported. The proportions of subjects with ≥1 local swelling event were 14%, 22%, and 15%, for periods 1, 2, and 3, respectively; no swellings were assessed as severe. For periods 1, 2, and 3, the proportions of subjects with ≥1 local AEs were 71%, 69%, and 56%, respectively; the proportions that discontinued due to AEs were 5%, 1%, and 3%; and the proportions with ≥1 local AEs requiring treatment were 4%, 4%, and 1%.

Conclusions: This study demonstrates that ragweed and grass SLIT-tablets can be co-administered safely.

Supported by Merck

Effects of Budesonide/Formoterol on Fixed Airflow Obstruction Status and Early Study Withdrawal Due to Predefined Asthma Events in Patients With Moderate to Severe Asthma

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Background: The effect of budesonide/formoterol (BUD/FM), BUD, or FM on fixed airflow obstruction (FAO) and withdrawal due to predefined asthma events (PAEs) is unclear.

Methods: This was a post-hoc analysis of a 12-week, randomized, placebo (PBO)-controlled study (NCT00652002) of patients aged ≥12 years with moderate–severe asthma. After 2-week run-in with twice-daily BUD 160 µg via pressurized metered dose inhaler (pMDI), patients received twice-daily BUD/FM pMDI 320/9 µg, BUD pMDI 320 µg, FM 9 µg via dry-powder inhaler, or PBO. Worsening asthma event criteria were predefined (PAEs; *Drugs.* 2006;66:2235-54). Postbronchodilator FAO status was assessed at screening, weeks 2, 6, and 12 via forced expiratory volume (FEV_1)/forced vital capacity (FVC) ratio for patients who completed the study. This analysis excluded patient withdrawals for any reason before week 2. Persistent FAO− (FEV_1/FVC ≥ lower limit of normal [LLN]) and persistent FAO+ (FEV_1/FVC <LLN) patients retained their FAO status at all visits. FAO status of variable patients was not consistent on all visits. FAO status and withdrawals due to PAEs were assessed.

Results: In 258/389 patients (66%), FAO status was persistent throughout the study (135 FAO− and 123 FAO+). The remaining 131 patients (34%) had variable FAO, changing status after screening. The percentage of patients with persistent FAO− (44%, 37%, 28%, and 30%), persistent FAO+ (30%, 29%, 35%, 33%), and variable FAO (26%, 34%, 38%, and 37%) differed in the BUD/FM, BUD, FM, and PBO groups, respectively. Overall, persistent FAO− patients had fewer PAEs than FAO+ or FAO variable patients. The numbers of patients who withdrew due to PAEs in the persistent FAO− (n = 2, 4, 3, and 7), persistent FAO+ (n = 1, 4, 15, and 15), or FAO variable (n = 6, 8, 15, and 12) classifications also differed for the BUD/FM, BUD, FM, and PBO groups, respectively.

Conclusions: Patients with moderate to severe asthma treated with BUD/FM are most likely to remain persistent FAO−, least likely to become FAO variable, and least likely to withdraw from the study if FAO+. Patients who were persistent FAO− vs persistent FAO+ or FAO variable had fewer withdrawals due to PAEs. Irrespective of FAO status, patients receiving BUD/FM experienced the fewest withdrawals due to PAEs.

Supported by AstraZeneca LP.

Sub-microgram Dose Formulations for Dose Ranging Studies With Long Acting Bronchodilators and Their Fixed Dose Combination Using Metered Dose Inhalers (MDIs)

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Introduction: Preliminary safety and efficacy studies with glycopyrrolate (GP; Reisner C, et al. *Eur Respir J* 2010; 36: Suppl. 54, 829s), formoterol fumarate (FF; Orevillo C, et al. *Eur Respir J* 2010; 36: Suppl. 54, 829s), and their fixed dose combination (GFF MDI, PT003), suggested the need to assess GP and GFF at sub-microgram levels before an appropriate dose for further evaluation in long term trials could be identified. Dose proportional and stable MDIs were prepared over a 120 fold dose range for GP, and 60 fold for GFF, with nanogram level precision using a novel cosuspension technology.

Methods: GP MDIs from 300 ng to 18 µg/actuation, FF MDIs from 480 ng to 9.6 µg, and GFF MDIs with GP doses of 600 ng to 18 µg/actuation at fixed FF dose of 4.8 µg/actuation, were prepared by cosuspending drug crystals in hydrofluoroalkane with spray-dried distearoyl-phosphatidylcholine porous particles. Aerodynamic particle size distribution (aPSD) and delivered dose uniformity (DDU) were tested at 30 L/min air flow. Robustness was tested by thermal cycling (−5.0°C to +40°C every six hours for 4 weeks), and isothermal storage at various temperatures.

Results: The in vitro drug delivery and aPSD for GP, in mono and combination MDIs with FF, were found to be linearly dose proportional ($r2 > 0.99$) over the entire dose range, wi**th stable aPSD and DDU. Similar performance was observed for FF MDIs.**

Conclusions: Pearl's novel cosuspension platform generates dose proportional and stable MDIs even with sub-microgram doses. Clinical studies evaluating an unprecedented dose range allowed for a complete benefit-risk assessment of GFF MDI, GP MDI and FF MDI.

Supported by AstraZeneca LP.

The burden of chronic hives (CH) from the patients' perspective as compared to psoriasis (PsO)

Susan Gabriel, Tom Karagiannis, Yunfeng Li, Vivian Herrera, Meryl Mendelson, Jeffrey Vietri, Patricia Russo

Introduction: Evidence on disease burden in persons with CH (proxy for chronic idiopathic urticaria) is scarce. We assessed CH burden of illness (BOI) relative to PsO, among US-based adults.

Methods: This retrospective cross-sectional study used self-reported data from the US National Health and Wellness Survey (1/2010-8/2012). BOI was defined by health-related QoL (SF12/36v2;SF6D), work productivity impairment (WPAI-GH) and healthcare resource use (prior 6 months). Comorbidity was measured using Charlson Comorbidity Index (CCI). Physician diagnosis included CH (n=747) or PsO (n=5107). PsO severity: based on percent body coverage (Mild:<3%; Moderate:3-10%; Severe:>10%).

Results: Comorbidity burden was highest for CH (CCI=1.05) and similar to Severe PsO (CCI=1.01). More persons with CH than PsO reported anxiety (41.6%), depression (38.8%), sleep difficulties (49.4%) and positive health indicators (never smoked [46.1%]; normal weight [29.1%]; exercise in prior month [64.5%;7.9 mean days]).

CH Physical and Mental Component Summary scores were 43.8 and 44.7, respectively (below population standard average [50]), and were similar to Moderate and Severe PsO, as were health utility scores (0.667 vs 0.671 and 0.651, respectively).

Less than 60% were active in the workforce. Persons with CH reported work productivity impairment similar to Moderate (overall work impairment: 28.9% vs 26.4%, respectively; activity impairment: 38.8% vs 36.8%) and Severe PsO (absenteeism: 8.6% vs 8.8%; presenteeism: 26.6% vs 27.6%). More persons with CH than PsO reported traditional HCP visits (92.4%) and ER/hospital use (20.7%/11.4% CH vs 14.5%/9.6% Severe PsO).

Conclusions: CH BOI is similar to or exceeds that of Moderate and Severe PsO, and should be considered when managing this condition.

Supported by Novartis

Cetirizine Improves Seasonal Allergic Rhinitis Symptoms in More Children than Loratadine and Placebo: A Responder Analysis

Authors: Mitesh Patel, Pharm D; Eduardo Urdaneta, MD; Qiong Du, MS; Mei-Miau Wu, Dr PH; Kathleen Franklin, BSN RN

INTRODUCTION: To evaluate seasonal allergic rhinitis (SAR) symptom response in children 2-12 years administered cetirizine and loratadine in placebo-controlled trials.

METHODS: Three 2-week randomized studies of cetirizine 5mg, cetirizine 10mg, loratadine 10mg and placebo were evaluated post-hoc for total symptom score complex (TSSC) changes. TSSC was sum of four or five SAR symptoms. Intention-to-treat subjects were evaluated, except 5 subjects with baseline TSSC=0. Treatment response was depicted by cumulative TSSC response curves for each study. Treatments were compared based on cumulative response curves and at ≥25%, ≥50%, and ≥75% improvement.

RESULTS: In all three studies, based on cumulative response curves, significantly more children in cetirizine 5mg and 10mg groups experienced symptom improvement than placebo subjects. In first study, significantly higher percentages of cetirizine 5mg-treated children had TSSC reductions at every quartile level of improvement than placebo-treated children. At ≥50% improvement, symptoms improved in 66.0% of cetirizine 5mg subjects and 35.8% of placebo subjects. In second and third studies, significantly more cetirizine 10mg subjects (37.1% and 19.3%, respectively) had ≥50% improvement than placebo subjects (19.7% and 13.6%, respectively). Compared with loratadine 10mg in third study, more children responded favorably to cetirizine 10mg overall. The difference was significant at ≥25% improvement.

CONCLUSIONS: In all three studies, significantly more children in cetirizine 5mg and 10mg groups experienced SAR symptom improvement based on cumulative response curves as well as at ≥50% improvement, compared with placebo subjects. Children taking cetirizine 5mg or 10mg had between 1.42-fold and 1.88-fold chance of achieving 50% or greater symptom improvement, compared with placebo.

Supported by McNeil

Treatment with Fel d 1 derived synthetic peptide immune-regulatory epitopes results in a persistent treatment effect on symptoms of cat allergy 2 years after treatment with 4 doses 4 weeks apart.

R.P. Hafner, P. Couroux, K. Armstrong, D. Patel[2], M. Larché

Background: Cat-peptide antigen desensitisation (Cat-PAD), the first in a new class of Synthetic Peptide Immuno-Regulatory Epitopes (SPIREs), showed a persistent treatment effect one year after the start of treatment in an Environmental Exposure Chamber (EEC) model of cat allergy (Patel et al., JACI 2013). In the current study, we evaluated the persistence of the treatment effect (tolerance) in the EEC model, two years after the start of treatment with 4 injections of Cat-PAD over a 12 week period.

Methods: 202 subjects were randomised to placebo, 8 x 3nmol Cat-PAD 2-weeks apart or 4 x 6nmol Cat-PAD 4-weeks apart; subjects attended EEC challenge at baseline and 18-22 weeks after the start of dosing. 89 subjects were enrolled into a follow on study and attended an EEC challenge at one year. Of these 50 subjects returned for a further follow-on study for EEC challenge at 100-104 weeks. Four nasal symptoms and 4 ocular symptoms were scored every 30 minutes, each on a scale of 0-3, and combined to give a Total Rhinoconjunctivitis Symptom Score (TRSS) on a scale of 0-24.

Results: Treatment with 4 x 6nmol Cat-PAD showed a mean change in the TRSS score at the two year EEC visit of -5.87 versus a change of -2.02 on placebo, ($p < 0.05$, Cat-PAD vs. placebo).

Conclusions: Treatment with 4 injections of Cat-PAD over a 12 week period showed a substantial reduction in subjects' cat allergy symptom scores in the EEC model that persisted two years after the start of treatment.

Supported by Ciraccia

Initial Evidence of Sustained Efficacy of House Dust Mite Synthetic Peptide ImmunoRegulatory Epitopes 2 Years After a Short Course of Treatment in House Dust Mite (HDM) Allergic Subjects

R Hafner, AM Salapatek, M Larche, B Ahenkorah, P Patel[2] and S Pawsey

Rationale: House Dust Mite Synthetic Peptide Immuno-Regulatory Epitopes (HDM-SPIRE) has previously been shown to significantly reduce rhinoconjunctivitis symptom scores in house dust mite (HDM) allergic individuals one year after a short course (4 doses in 12 weeks) of treatment. In this study, subjects returned to evaluate continued efficacy two years after the start of treatment.

Methods: 72 of the 116 subjects who had previously participated in the one year randomised, double-blind, placebo-controlled study underwent exposure to HDM allergen in an exposure chamber ~2 years after starting a short course (4 or 11 doses) of HDM-SPIRE or placebo. No further drug was administered. Symptom scores were recorded during the 4-hour exposure period on three consecutive days and were compared to time-matched symptom scores from a baseline (pre-dosing) assessment.

Results: The mean reduction in symptom scores over the 3 days (pre-specified endpoint) in subjects receiving 4 doses of HDM-SPIRE (-6.49±4.28) was greater than the reduction in placebo subjects (-4.70±3.71). The 4 dose regimen out-performed the 11 dose regimen in this analysis. Subjects with more severe symptoms at baseline had an even greater reduction in symptom scores in the 4 dose HDM-SPIRE group (-7.59±4.10) than the placebo group (-4.92±4.09).

Conclusion: Despite a marked placebo effect, 4 doses of HDM-SPIRE 12 nmol was associated with a clear trend towards persistence of efficacy 2 years after dosing. This persistence of effect should be confirmed in larger studies. HDM-SPIRE is a potentially exciting new treatment for HDM allergy.

Supported by Ciraccia

Designing Auto-Injectors: Effect of Form Factor on the Human Factors of Efficient Drug Delivery in Adults and Children

A Barbir, JT Dennerlein[1]

INTRODUCTION: Effective drug delivery through epinephrine auto-injectors (EAIs) is essential during anaphylaxis. Physical form factor can influence drug delivery by affecting the applied force of the device; thus, we evaluated EAI form factor effectiveness and preference in adults and children.

METHODS: Epinephrine auto-injectors with 3 form factors (cylindrical, elliptical, and prismatic) were tested in a laboratory-based repeated measures experiment with adults (n=20; aged 18-30 years) and children (n=20; aged 8-12 years). Participants applied their maximum possible force onto a force plate positioned over their thigh (maximum force capability task) and practiced an injection using the EAI trainer after watching the device's training video (application task). Participants also rated force confidence and preference.

RESULTS: The elliptical device exhibited the greatest axial applied force (P=0.0083) and force transmission (P<0.0001) in adults. Similarly, the elliptical device produced the greatest axial applied force in children (P=0.0084), although both the cylindrical and elliptical devices yielded the highest force transmission (1.4 N/%MVC; P=0.0008) when compared with the prismatic device (1.1 N/%MVC). In adults, force confidence was highest with the cylindrical and elliptical devices (P<0.0001), whereas there were no significant differences in force confidence in children. Overall, adults preferred the elliptical device (60%) followed by the cylindrical (25%) and prismatic devices (15%), whereas children equally preferred the elliptical and prismatic devices (45%) over the cylindrical device (10%).

CONCLUSIONS: Data from these studies reveal similar trends in EAI effectiveness and preference in both adults and children and suggest that the elliptical form may have better drug delivery.

Supported by Mylan

EPIPEN4SCHOOLS® Survey: Characteristics and Treatment of Anaphylactic Events in a US School Setting

MV White, S Silvia, K Hollis, M Wooddell, S Hogue

INTRODUCTION: The EPIPEN4SCHOOLS® program was launched in 2012 to provide EpiPen® Auto-Injectors free of charge to qualifying public and private kindergarten, elementary, middle, and high schools in the United States.

METHODS: This exploratory, cross-sectional, web-based survey examined the characteristics and treatment of anaphylactic events in US schools participating in the EpiPen4Schools program.

RESULTS: A total of 919 anaphylactic events were reported by 11% of schools that responded to questions on the occurrence of anaphylaxis (607/5683). Most anaphylactic events occurred in students (89%, 757/852), and 22% (187/852) occurred in individuals with no known allergies. Triggers were reported for 92% of anaphylactic events (847/919). The most common triggers were food (62%, 529/847) and insect stings (10%, 81/847); however, triggers could not be identified in 20% of events (172/847). Epinephrine auto-injectors (EAIs) were used in 75% of events with data on treatment administration (636/851). Most of the remaining events were treated with antihistamines (18%, 157/851). Of the events treated with EAIs, the school's stock EpiPen Auto-Injector or the individual's personal EpiPen Auto-Injector was used to treat 49% (310/636) and 45% of events (289/636), respectively; 6% of events (37/636) were treated with other types of EAIs or EAIs of unknown source.

CONCLUSIONS: In the EpiPen4Schools survey, high proportions of observed anaphylactic events had unknown triggers or were experienced by individuals with no known allergies. Nearly 25% of events were not treated with epinephrine, the first-line therapy for anaphylaxis. These data demonstrate the unpredictable nature of anaphylaxis and the importance of preparedness training in schools.

Supported by Mylan

Dupilumab Improves Lung Function and Reduces Severe Exacerbations in Uncontrolled Asthmatics with Baseline Eosinophil Levels Above and Below 300 cells/µL

Sally Wenzel, MD, Lin Wang, PhD, E. Rand Sutherland, MD, MPH, Robert R. Evans, PharmD, Ariel Teper, MD

INTRODUCTION: Dupilumab inhibits both IL-4 and IL-13 signaling. The aim of this interim analysis was to evaluate the efficacy and safety of different dupilumab regimens in patients with uncontrolled asthma at 12 weeks.

METHODS: Multinational, 24-week, double-blind, dose-ranging study in adults with uncontrolled asthma, while on medium to high-dose ICS/LABA (ClinicalTrials.gov: NCT01854047). Randomized patients were stratified according to baseline eosinophil counts. The primary outcome was FEV_1 change from baseline at Week 12 in patients with high eosinophil count (HEos; ≥300/µL). Secondary endpoints included annualized severe exacerbation rate, change in FEV_1 for all patients (intent-to-treat [ITT] population), and safety.

RESULTS: 776 patients were randomized, 63% were female, mean age was 48.6 years, 325 (42%) had HEos, mean baseline % predicted FEV_1 (SD) was 61% (11%), mean baseline ACQ-5 (SD) was 2.74 (0.81). Dupilumab showed significant improvements in FEV_1 at Week 12 in patients with HEos versus placebo at all doses ($p<0.03$) except 200 mg q4w. Dupilumab significantly reduced annualized severe exacerbation rates at all doses ($p<0.01$) except 300 mg q4w, across all subgroups. The 200 mg q2w and 300 mg q2w regimens demonstrated significant reductions in exacerbation risk (ITT population: 67–68%, $p\leq0.001$; HEos group: 64–75%, $p<0.05$). Adverse events (AEs) were balanced across treatment groups (70–74% vs 67% with placebo); injection site reaction was the most common AE (13–25% with dupilumab vs 12% with placebo).

CONCLUSIONS: Dupilumab improved lung function as measured by FEV_1, and reduced the annualized severe exacerbation rate in patients with uncontrolled moderate-to-severe asthma.

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