

# North American Rhinology & Allergy Conference January 14-17, 2016 – St Thomas, VI

All Scientific Posters will be on display in the Grand Harbour II Ballroom beginning Friday morning. Authors of these posters are requested to be at their poster to discuss their work from 10:00-11:00am, Friday and Saturday.

Posters not for  
CME credit

## ASSESSMENT OF TASTE DISTORTION WITH FLUNISOLIDE HFA (AEROSPAN®) IN PATIENTS WITH MILD-TO-MODERATE ASTHMA

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**Introduction:** A total of 833 patients with mild-to-moderate asthma were treated with flunisolide HFA in two 12-week efficacy trials (adults  $\geq 12$  years and children 4 – 11 years, respectively) and in two 52-week safety trials in these age groups. The objective of this evaluation was to assess the reports of taste distortion in these trials.

**Methods:** In the two 12-week trials, patients were treated for 2 weeks with flunisolide CFC and then randomized to: flunisolide HFA 80 mcg (1 puff; ped and adult trials), HFA 160 mcg (2 puffs; ped and adult trials), HFA 320 mcg (4 puffs, adult trials only), or placebo BID. In the two 52-week trials, patients received flunisolide HFA dosages ranging from 160 mcg (80 mcg BID) to 640 mcg (320 mcg BID).

**Results:** In the 12-week trials, 0 (0%) of 519 asthma patients discontinued treatment with flunisolide HFA due to taste distortion. Overall, 8 (1.5%) of those 519 patients in the 12-week trials treated with flunisolide HFA experienced taste distortion, with no apparent dose-related increases (80 mcg BID = 1.6%; 160 mcg BID = 1.8%; 320 mcg BID = 0.9%; placebo BID = 0.5%). No differences in incidence were seen based on age, gender or race. Within the 52-week trials, 4 (1.3%) of 314 asthma patients discontinued treatment with flunisolide HFA due to taste distortion.

**Conclusions:** Flunisolide HFA dosages of up to 320 mcg BID were well tolerated regarding taste. Taste distortion was not dose related and few patients experienced or discontinued treatment due to problems with taste.

## SAFETY AND EFFICACY OF MP-AZE-FLU (DYMISTA®) NASAL SPRAY COMPARED WITH FLUTICASONE PROPIONATE NASAL SPRAY IN PEDIATRIC PATIENTS WITH ALLERGIC RHINITIS: RESULTS OF RANDOMIZED, CONTROLLED TRIALS

Renee Bomar, MSN, CPNP; Todd Mahr, MD; William Berger, MD; Ellen Sher, MD

**Introduction:** MP-AzeFlu (Dymista) is a single intranasal formulation of azelastine HCL and fluticasone propionate for the treatment of seasonal allergic rhinitis (SAR). Two randomized, controlled studies were conducted to evaluate safety and efficacy of MP-AzeFlu in pediatric patients  $\geq 4$  years to  $< 12$  years of age with SAR.

**Methods:** The first study was an open-label, 3-month safety trial, which randomized patients 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. The second study was a 2-week, randomized, double-blind, placebo-controlled efficacy trial. Change from baseline in the 12-hr reflective total nasal symptom score (rTNSS) was the primary endpoint. Patients were randomized to treatment with MP-AzeFlu (n=173) or placebo (n=175). In both studies, patients were stratified by age: (1)  $\geq 4$  years to  $< 6$  years; (2)  $\geq 6$  years to  $< 9$  years; and (3)  $\geq 9$  years to  $< 12$  years.

**Results:** In the safety 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 diarrhea (1% and 4%). Discontinuation rate due to AEs was 2% with MP-AzeFlu and 4% with FP. There were no findings of nasal mucosal ulceration or septal perforation. In the 2-week efficacy study, there was a significant (P=.02) change from baseline in rTNSS favoring MP-AzeFlu over placebo among patients compliant with protocol requirements.

**Conclusions:** MP-AzeFlu was effective and well-tolerated when administered as 1 spray per nostril twice daily in pediatric patients with SAR.

## IN VITRO CHARACTERIZATION OF FLUNISOLIDE HFA (AEROSPAN®) PARTICLE SIZE AND PARTICLE DISTRIBUTION

Alexander D'Addio, PhD; Eli Meltzer, MD

**Introduction:** The objective of these experiments was to determine the aerodynamic particle size distribution (APSD) of flunisolide HFA (80  $\mu\text{g}$ /actuation) with built-in spacer (Aerospan) compared to fluticasone propionate (Flovent, 110  $\mu\text{g}$ /actuation) with valved holding chamber (F/VHC) and without VHC (F) and beclomethasone (QVAR, 40  $\mu\text{g}$  and 80  $\mu\text{g}$ /actuation) with valved holding chamber (Q/VHC, 80  $\mu\text{g}$  only) and without VHC (Q for 40 and 80  $\mu\text{g}$ ).

**Methods:** Mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD), fine particle mass (FPM [ $\leq 5.0 \mu\text{m}$ ][ $\mu\text{g}/\text{shot}$ ]), dose delivered to impactor, fine particle fraction (FPF [% dose to impactor]), and fine particle fraction (FPF [%ND]) were calculated. Percent nominal dose (%ND) was calculated as measured dose to impactor/claimed nominal dose.

**Results:** Flunisolide HFA mean MMAD was  $1.2 \pm 0.1 \mu\text{m}$ . F/VHC and F MMADs were  $2.3 \pm 0.1 \mu\text{m}$  and  $2.6 \pm 0.1 \mu\text{m}$ , respectively. Q/VHC and Q MMADs were  $0.9 \pm 0.1 \mu\text{m}$  and  $1.0 \pm 0.1 \mu\text{m}$ , respectively for 80  $\mu\text{g}$  and  $0.9 \pm 0.0 \mu\text{m}$  for the 40  $\mu\text{g}$  dose without VHC. FPM was highest (77  $\mu\text{g} \pm 2 \mu\text{g}$ ) with flunisolide HFA compared to F/VHC (57  $\pm 9 \mu\text{g}$ ) and F (50  $\pm 9 \mu\text{g}$ ). FPF with flunisolide HFA (92.6%) was comparable to F/VHC (87.3%) and nearly twice that of F (46.5%). 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  $\mu\text{g}$  only - 81.4%) and Q (80  $\mu\text{g}$  - 70.2%; 40  $\mu\text{g}$  - 70.4%).

**Conclusions:** 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.

## IN VITRO DETERMINATION OF THE ROBUSTNESS OF THE EMITTED DOSE OF FLUNISOLIDE HFA PMDI

Alexander D'Addio, PhD; David Skoner, MD; Daniela Bräutigam; Eli Meltzer, MD

**Introduction:** These experiments were designed to determine the robustness of the aerosol characteristics of the delivered dose of Aerospan® 80  $\mu\text{g}$  compared to QVAR® 80  $\mu\text{g}$  when used according to the prescribing information.

**Methods:** The test drugs were administered through an Alberta idealized throat model with a realistic flow profile (30 L/min) generated by a Copley BRS3000 breathing simulator. The amount of drug deposited on the actuator/spacer, the throat, and the filter of the aerosol sampler was determined by HPLC analysis.

**Results:** Aerospan provided higher amount of drug on the filter than QVAR and achieved the labeled dose (80  $\mu\text{g}$ ) when sampled simultaneously with actuation. The amounts of flunisolide reaching the filter/percent of labeled dose were: 78.3  $\mu\text{g}/97.9\%$  when actuated simultaneously with sampling, 70.1  $\mu\text{g}/87.6\%$  at 1 sec after, 66.0  $\mu\text{g}/82.5\%$  at 2 sec after, and 68.3  $\mu\text{g}/85.4\%$  at 3 sec after sampling. QVAR did not achieve the labeled dose (80  $\mu\text{g}$ ) with simultaneous actuation (55.5  $\mu\text{g}/69.4\%$ ) or at any interval thereafter. The percentage of drug recovered on the throat relative to the emitted (ex-valve) dose was 5.8% or lower for Aerospan compared to 17.6% or higher for QVAR.

**Conclusions:** When inhalation is performed as instructed by the prescribing information the amount of drug on the filter is higher with Aerospan than with QVAR, suggesting a potential higher lung deposition with Aerospan. Actuation delay of up to 3 sec after start of inhalation does not significantly impact the aerosol characteristics of Aerospan confirming robustness and reliability of drug delivery.

**Efficacy of 300IR 5-Grass Pollen Sublingual Tablet (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract) in the Treatment of Rhinitis and Ocular Symptoms in Polysensitized Subjects with Grass Pollen-Induced Allergic Rhinoconjunctivitis**

Linda S. Cox, MD, Peter S. Creticos, MD, Yann Amistani, MD, Josiane Cognet-Sicé, MD, Kathy Abiteboul, MD

**Rationale:** The 300IR 5-grass pollen sublingual tablet administered to subjects with grass pollen-induced allergic rhinoconjunctivitis (ARC) has consistently proven efficacious across the development program. Here we present efficacy data on individual rhinitis and ocular symptoms in polysensitized subjects.

**Methods:** Subjects with medically confirmed grass pollen-induced ARC for  $\geq 2$  years were enrolled in one of 4 natural field studies. All underwent prick skin testing to 5-grass mix or timothy and a panel of geographically relevant aeroallergens. Those testing positive to 5-grass/ timothy and at least one other allergen were considered polysensitized. Daily, subjects self-scored each of their rhinitis and ocular symptoms (sneezing, rhinorrhea, nasal pruritus, nasal congestion, ocular pruritus, watery eyes) scaled from 0 (none) to 3 (severe). Individual symptom scores, Rhinitis Total Symptom Score (RTSS, the sum of the four rhinitis scores) and Conjunctivitis Total Symptom Score (CTSS, the sum of the two ocular scores) were analyzed descriptively.

**Results:** Of 1,381 subjects whose data were analyzed, 891 (65%) were polysensitized (300IR=427; placebo=464). In this subset, individual symptom scores were significantly and consistently lower in the 300IR group than in the placebo group with relative mean differences from placebo of -15% (sneezing), -19% (rhinorrhea), -22% (nasal pruritus), 24% (nasal congestion), 31% (ocular pruritus) and -36% (watery eyes). Significant reductions of 20% and 33% from placebo were also demonstrated in overall RTSS and CTSS, respectively. One subject reported a severe hypersensitivity reaction and recovered with oral corticosteroid and antihistamine.

**Conclusions:** Treatment with 300IR 5-grass pollen sublingual tablet effectively reduced all rhinitis and ocular symptoms in polysensitized subjects with grass pollen-induced ARC.

**Quality of Life Improvement in Adults across the Clinical Development Program of 5- Grass Pollen Sublingual Tablet (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract)**

Linda S. Cox, MD, Peter S. Creticos, MD, Yann Amistani, MD, Josiane Cognet-Sicé, MD, Kathy Abiteboul, MD

**Rationale:** The efficacy of 4-month pre- and co-seasonal treatment with 5-grass pollen sublingual tablet was demonstrated in subjects with grass pollen-induced allergic rhinoconjunctivitis (ARC). Here, we present Quality of Life (QoL) data across three Phase III studies.

**Methods:** Three randomized, double-blind, placebo-controlled studies (two single-season and one long-term) were conducted in USA, Canada, Europe and Russia. Adults (18-65 years) with grass pollen-induced ARC received placebo or a 300IR 5-grass tablet daily, 4-month preseasonally and over the pollen season. Subject-reported Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores, evaluated on a 7-point scale, were recorded before and midway through each pollen season. Lower scores indicate better QoL. ANCOVA analysis was performed.

**Results:** Of 1,210 randomized subjects, 1,051 (300IR=500; placebo=551) could be included in the analysis. Across studies, significant differences ( $p < 0.01$ ) in the overall RQLQ mean scores were consistently observed at the expected peak of pollen season between the 300IR and placebo groups: -0.32, CI95% [-0.55;0.10] (Study 1), 0.29, CI95% [-0.51;-0.08] (Study 2) and -0.29, CI95% [0.48;- 0.10] (Long-Term study Year 1). This reflected relative improvements vs. placebo of 20.6%, 20.9% and 17.6%, respectively. In the Long-Term study, RQLQ mean score differences from placebo were 0.41, CI95% [0.64;- 0.19] ( $p < 0.001$ ) in the third treatment year, 0.47, CI95% [0.70; 0.23] ( $p < 0.001$ ) in the first year post-treatment, corresponding to relative improvements of 30.5% and 32.9%, respectively. Severe hypersensitivity reaction, severe laryngeal edema and gastroenteritis were reported by three subjects.

**Conclusions:** Treatment with 5-grass pollen sublingual tablets improved QoL in grass pollenallergic adults. Results were consistent across countries and over three years of treatment.