

**790** Intra-Nasal Theophylline for the Treatment of Chronic Anosmia and Hyposmia

Marc F. Goldstein, MD, FAAAAI<sup>1</sup>, Gregory J. Hilditch<sup>2</sup>, Ina Frankel, BS<sup>3</sup>, Lauren Chambers, BA<sup>1</sup>, Donald J. Dvorin, MD, FAAAAI<sup>4</sup>, and George Belecanech, MD<sup>1</sup>; <sup>1</sup>Allergic Disease Associates, PC, Philadelphia, PA, <sup>2</sup>Drexel University College of Medicine, Philadelphia, PA, <sup>3</sup>Allergic Disease Associates, PC, Philadelphia, PA, <sup>4</sup>Allergic Disease Associates, PC, Medford, NJ.

**RATIONALE:** To evaluate the efficacy of intra-nasal theophylline therapy (ITp) in improving smell in subjects with chronic hyposmia/anosmia.

**METHODS:** Ten subjects with chronic hyposmia/anosmia were evaluated for smell loss, with history and physical, nasopharyngolaryngoscopy, laboratory tests, allergy skin tests, paranasal sinus CT, prednisone challenge, and brain MRI. Subjects completed a University of Pennsylvania Smell Identification Test (UPSIT) Monell-Jefferson Taste and Smell Questionnaire (M-JTSQ) pre and post-ITp to evaluate smell function quantitatively and qualitatively. Subjects consented to an open-label pilot study with 20µg theophylline/0.4mL saline solution administered by 4 sprays in each nostril daily for 1 month. Complete responders (CR) and partial responders (PR) to ITp continued on long-term ITp.

**RESULTS:** Two of 10 subjects dropped out of the study with limited exposure to ITp and were excluded from analysis. Post-ITp, 2 of 8 subjects were considered CR; these subjects showed improvement in their UPSIT score and M-JTSQ responses. Two of 8 subjects were considered PR; these subjects showed improvement in either UPSIT score or M-JTSQ responses. CR's and PR's were monitored on long-term ITp and reported persistent improvement. CR's and PR's did not differ significantly from non-responders in pre ITp clinical or laboratory characteristics or response to prednisone challenge. No adverse effects to ITp were reported by any subjects.

**CONCLUSIONS:** ITp improved smell in 50% of subjects after 4 weeks of ITp; continued ITp improved smell for up to 27 months. Pre-treatment subject phenotype did not predict treatment response. Response to prednisone did not predict response to ITp ( $r = 0.58$ ).

**791** Oral Cetirizine 10mg Significantly Improves Highest Perennial Allergic Rhinitis Symptom Severity Score(s) in Posthoc Analysis

Mitesh Patel, PharmD<sup>1</sup>, Mei-Miau Wu, Dr, PH<sup>2</sup>, Harshini Turner, MBBS<sup>1</sup>, and Kathleen Franklin, BSN, RN<sup>1</sup>; <sup>1</sup>Johnson & Johnson Consumer Inc., McNeil Consumer Healthcare, Fort Washington, PA, <sup>2</sup>Johnson & Johnson Consumer Products US, Morris Plains, NJ.

**RATIONALE:** The effect of oral cetirizine 10mg on subjects' highest (worst) perennial allergic rhinitis (PAR) symptom severity score(s) was evaluated in a posthoc analysis of randomized controlled trial (RCT) data.

**METHODS:** Subjects (aged  $\geq 12$  years) rated severity for 6 or 7 PAR symptoms, including sneezing, runny nose, itchy nose, postnasal drip, itchy eyes, watery eyes, and itchy mouth, daily in three RCTs of cetirizine 10mg or placebo. Symptom(s) with the highest baseline score were predefined as the individual's worst symptom(s) in the posthoc analysis. When multiple symptoms shared the same highest baseline score, the daily average of ratings was calculated to represent the post-baseline rating of subjects' worst symptom(s). Daily ratings of worst symptom(s) were averaged over 4 weeks. The efficacy endpoint was the change from baseline worst symptom severity score(s). Data from subjects with baseline symptom severity scores  $\geq 1$  (0=none, 3=severe) were evaluated.

**RESULTS:** In these subjects, mean baseline worst symptom scores were 2.39 (SD=0.49; range 1.0-3.0, N=308) in the cetirizine group and 2.40 (SD=0.50; range 1.0-3.0, N=313) in the placebo group ( $P=0.691$  between groups). Over 4 weeks, the LS mean change from baseline worst symptom score(s) for cetirizine was -1.03 (SE=0.04, N=307) and -0.82 (SE=0.04; N=312) for placebo ( $P<0.001$  versus placebo). The percent difference in relief achieved with cetirizine 10mg was 26.1% compared with placebo.

**CONCLUSIONS:** Oral cetirizine 10mg significantly improved the severity of subjects' worst symptom(s), including sneezing, runny nose,

itchy nose, postnasal drip, itchy eyes, watery eyes, and itchy mouth, in adults with PAR.

**792** Intranasal Azelastine and Mometasone Exhibit a Synergistic Effect on a Murine Model of Allergic Rhinitis

Soo Whan Kim; The Catholic university of korea, Seoul, Korea, The Republic of.

**RATIONALE:** The purpose of this study was to compare the anti-allergic effects of the combination of azelastine and mometasone with those of either agent alone in a *Dermatophagoides farinae* (Derf)-induced murine model of allergic rhinitis (AR).

**METHODS:** Forty BALB/c mice were divided into five groups: azelastine (A), mometasone (M), a combination of azelastine and mometasone (MA), Derf, and control. Derf served as the allergen. Allergic symptom scores, eosinophil counts, and serum Derf-specific IgE levels were measured. The mucosal levels of mRNAs encoding interferon (IFN)- $\gamma$ , T-bet, interleukin (IL)-4, GATA-3, Foxp3, IL-17, and ROR- $\gamma$ t were determined by real-time polymerase chain reaction. The T-bet, GATA-3, Foxp3, and ROR- $\gamma$ t results were confirmed by Western blotting.

**RESULTS:** Nose-rubbing motions; the levels of mRNAs encoding IL-4, GATA-3, and ROR- $\gamma$ t; and tissue eosinophil count were reduced in the MA compared with those in the Derf group (all  $P$  values  $<0.05$ ). The levels of mRNAs encoding GATA3 and IL-4 mRNA [synthesized by T helper (Th)2 cells] were reduced and that of mRNA encoding Foxp3 was increased in the MA compared with those in the Derf and A groups. Western blotting confirmed these findings.

**CONCLUSIONS:** We found that the combination of intranasal azelastine and mometasone synergistically suppressed Th17 responses and (reciprocally) elevated Treg responses. Therefore, this combination not only ameliorated allergic inflammation by suppressing Th2 responses, but also usefully modified the Treg/Th17 balance.

**793** Efficacy Analysis of MP-AzeFlu Compared with Fluticasone Propionate Nasal Spray in Children 6 through 11 Years of Age with Allergic Rhinitis

Ellen R. Sher, MD, FAAAAI<sup>1</sup>, and William E. Berger, MD, MBA<sup>2</sup>; <sup>1</sup>Atlantic Allergy, Asthma and Immunology Associates, Ocean, NJ, <sup>2</sup>Allergy & Asthma Associates of Southern California, Mission Viejo, CA.

**RATIONALE:** MP-AzeFlu (Dymista®) is a novel intranasal formulation of azelastine hydrochloride (AZE) and fluticasone propionate (FP) for treatment of allergic rhinitis. The objective of the current analysis was to evaluate the efficacy of MP-AzeFlu compared to FP administered 1 spray per nostril twice daily in children 6 through 11 years of age.

**METHODS:** This was a randomized, open-label, 3-month safety study in patients 4 through 11 years of age. Qualified patients 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. Randomization was in a 3:1 ratio (MP-AzeFlu [n=304]:FP [n=101]). Efficacy was not a pre-specified study objective but was evaluated by self-assessment of overall allergy symptom severity in a subset of patients 6 through 11 years (MP-AzeFlu [n=264]:[FP: n=89]). Symptom severity was scored on a 4-point scale from 0 to 3 (0 = none; 1 = mild; 2 = moderate; 3 = severe).

**RESULTS:** Total symptom score at baseline was 1.73 in the MP-AzeFlu group and 1.80 in the FP group (max score: 3). Over the entire study period, patients treated with MP-AzeFlu experienced a -0.68 pt reduction in overall symptom score (corresponding to a -5.44 change from baseline in AM + PM reflective total nasal symptom score (rTNSS; max = 24), significantly greater relief than that afforded by FP (-0.54 pt reduction; Diff: -0.14; 95% CI: -0.28, -0.01;  $p=0.04$ ).

**CONCLUSIONS:** MP-AzeFlu provided significantly greater relief of AR symptoms than FP in children 6 through 11 years of age.