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153 Effect of Simvastatin on Transforming Growth Factor BETA-1-Induced Myofibroblast Differentiation and Collagen Production in Nasal Polyp-Derived Fibroblasts
Il-Ho Park, MD, and Heung-man Lee, MD, PhD. Department of otorhinolaryngology-head and neck surgery, Korea university college of medicine, Seoul, South Korea.

Background: Statins are the most commonly prescribed drugs for the treatment of hypercholesterolemia. Statins exert not only lipid-lowering but also other cellular effects, including anti-fibrotic properties. The purposes of this study were to determine the effect of simvastatin on Transforming growth factor (TGF)-β1-induced myofibroblast differentiation and collagen production in nasal polyp-derived fibroblasts (NPDFs) and to verify the mechanism of the effect of simvastatin in TGF-β1-induced myofibroblast differentiation in NPDFs.

Methods: NPDFs were pre-treated with simvastatin with or without mevalonate or Y-27632 for 2 hours prior to induction by TGF-β1. The expression of α-smooth muscle actin (SMA) and collagen type IV mRNA was determined by a reverse transcription-polymerase chain reaction, and the expression of α-SMA protein was determined by immunofluorescent cytochemical staining. Total soluble collagen production was analyzed by the SirCol collagen dye-binding assay. Phosphorylation of Smad 2/3 was evaluated by Western blot analysis.

Results: In TGF-β1-induced NPDFs, simvastatin significantly inhibited the expressions of α-SMA and collagen type IV mRNA and reduced α-SMA and collagen protein levels. Pre-treatment with mevalonate reversed the effect of simvastatin. The expression of α-SMA mRNA and protein was significantly decreased by pre-treatment with Y-27632. The TGF-β1-induced expression of pSmad 2/3 protein was notably decreased by pre-treatment with simvastatin.

Conclusions: We showed that simvastatin inhibits TGF-β1-induced myofibroblast differentiation (expression of α-SMA) and collagen production in NPDFs and Rho/ROCK and TGF-β1/Smad signaling is involved in an underlying mechanism. The results of our study suggest that simvastatin is a possible candidate for the suppression of nasal polyp formation.

154 A 26-Week Study Evaluating the Safety and Efficacy of Ciclesonide Hydrofluoralkane Nasal Aerosol in Subjects With Perennial Allergic Rhinitis
William Berger, MD, MBA,1 Dale Mohar, MD,2 Gordon Raphael, MD,3 Craig LaForce, MD,4 Holly Huang, PhD, MPH,5 Shailesh Desai, PhD,5 Frederick Bode, MD,2 and John Karamfilidis, PharmD6.1 Allergy & Asthma Associates, Mission Viejo, CA; 2Kerrville Research Associates, Kerrville, TX; 3Kerrville Research Associates, Kerrville, TX; 4Kerrville Research Associates, Kerrville, TX; 5Clinical Research, Raleigh, NC; 6Sunovion Pharmaceuticals, Inc., Marlborough, MA.

Background: Ciclesonide hydrofluoralkane nasal aerosol (CIC-HFA) is currently in development as a potential treatment for allergic rhinitis. The objective of this study was to determine the long-term safety and efficacy of CIC-HFA compared to placebo in subjects with perennial allergic rhinitis (PAR).

Methods: Subjects ≥12 years of age with a ≥2 year history of PAR were randomized in a placebo-controlled, double-blind, parallel group, multicenter study to CIC-HFA 74 μg (N = 298), CIC-HFA 148 μg (N = 505), or placebo (N = 307) QD AM for 26 weeks. Subject-reported change from baseline in reflective total nasal symptom score (rTNSS) and instantaneous total nasal symptom score (iTNSS) averaged every 2 weeks over the 26 weeks of the treatment period were secondary endpoints and were calculated as a sum of the individual nasal symptoms of congestion, runny nose, sneezing, and nasal itching. Change from baseline in the individual reflective and instantaneous nasal symptom scores averaged every 2 weeks over the 26 weeks of treatment period were also evaluated. Treatment-emergent adverse events (TEAEs) were assessed throughout the study.

Results: CIC-HFA 74 μg and CIC-HFA 148 μg doses demonstrated improvement in rTNSS (LS mean change 0.65 & 0.52 respectively, P ≤ 0.01 for both), iTNSS (LS mean change 0.51 & 0.42 respectively, P ≤ 0.05 for both), and improvements in the individual reflective and instantaneous nasal symptoms (P ≤ 0.05 for all except instantaneous sneezing for the CIC-HFA 74 μg dose) at 26 weeks from baseline. P values were unadjusted for multiplicity. The overall incidence of TEAEs was comparable between the CIC-HFA treatment groups and placebo. The most frequently reported TEAEs (≥5% of subjects in any treatment group) were headache, nasopharyngitis, upper respiratory tract infections, viral upper respiratory tract infections, sinusitis, and epistaxis.

Conclusions: In this study, once-daily treatment with CIC-HFA 74 μg or CIC-HFA 148 μg demonstrated improvements in the nasal symptoms of PAR. Both active treatments were well tolerated.

155 Omalizumab Improves Asthma but not Nasal Symptoms in Japanese Patients With Severe Allergic Asthma and Rhinitis
Fuyumi Nishihara, MD, Yotaor Takaku, MD, PhD, Kazuyuki Nakagome, MD, PhD, Takehito Kobayashi, MD, PhD, and Makoto Nagata, MD, PhD. Allergy Center, Department of Respiratory Medicine, Saitama Medical University, Moroyama-Machi, Japan.

Background: There is evidence that humanized monoclonal antibody against IgE (Omalizumab) is effective in severe allergic asthma. In this study, we examined the effectiveness of omalizumab on asthma and nasal symptoms in Japanese patients with severe allergic asthma and rhinitis.

Methods: An open-label study that enrolled 7 patients with both severe allergic asthma and rhinitis who visited Allergy Center, Saitama Medical University was performed. All patients presented uncontrolled asthma despite medication including high-dose inhalational corticosteroids, long-acting beta2-agonist, leukotriene receptor antagonist, theophylline, and oral prednisolone. Omalizumab was added on their treatments and symptoms score using Asthma Control Test (ACT), peak expiratory flow rate (PEFR), exhaled nitric oxide (eNO), sputum eosinophils and nasal symptoms were evaluated before and 12 to 16 weeks after omalizumab.

Results: Omalizumab significantly improved ACT scores especially dose of rescue use of short-acting beta2-agonist (P < 0.05) and PEFR (P < 0.05). Furthermore, omalizumab significantly decreased exhaled both eNO (P < 0.05) and the percentage of eosinophils in induced sputum. On the other hand, nasal symptoms were not change following induction of omalizumab.

Conclusions: Clinical effectiveness of omalizumab was confirmed in Japanese population of severe allergic asthma, but not rhinitis. The therapeutic potency of omalizumab on asthma likely involves anti-inflammatory properties such as decreasing eNO or airway eosinophilia.

156 Economic Evaluation of Grass Tablets for Immunotherapy (oralair) Compared to Placebo in Adults and Children in Italy
Amerigo Cicchetti,1 Matteo Ruggieri,1 Alessandro Fiocchi, MD,2 Sergio Bonini, MD,3 Paolo Puccinelli,4 Giovanni Passalacqua, MD,5 and Franco Frati, MD6.1 Faculty of Economy, Catholic University, Rome, Italy; 2Melloni Paediatrics, Milano, Italy; 3Second University of Naples, Rome, Italy; 4Stallergenes Milan, Milano, Italy; 5Allergy & Respiratory