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**Effect of Simvastatin on Transforming Growth Factor BETA-1-Induced Myoﬁbroblast Differentiation and Collagen Production in Nasal Polyprop-Derived Fibroblasts**

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**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-27643 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 Sirius 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 as an underlying mechanism. The results of our study suggest that simvastatin is a possible candidate for the suppression of nasal polyp formation.

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**A 26-Week Study Evaluating the Safety and Efficacy of Ciclesonide Hydroﬂuoralkane Nasal Aerosol in Subjects With Perennial Allergic Rhinitis**

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**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 (tTNSS) 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 demonstrated improvement in iTNSS (LS mean change 0.65 & 0.42 respectively, P ≤ 0.05 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 not adjusted 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.

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**Omalizumab Improves Asthma but not Nasal Symptoms in Japanese Patients With Severe Allergic Asthma and Rhinitis**

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**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 beta-2 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.

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**Economic Evaluation of Grass Tablets for Immunotherapy (oralair) Compared to Placebo in Adults and Children in Italy**

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**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 beta-2 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.