606 Long-term Safety and Tolerability of Two Doses of Mometasone Furoate/Formoterol (MF/F) Combination, Administered Via a Metered-dose Inhaler, for the Treatment of Moderate-to-severe Persistent Asthma

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RATIONALE: The combination of mometasone furoate and formoterol (MF/F) administered via a single metered-dose inhaler (MDI) is in development for the treatment of asthma. We report findings from a randomized, parallel-group, multicenter, open-label, evaluator-blinded study assessing the long-term safety of medium- and high-dose MF/F compared to fluticasone propionate/salmeterol MDI (F/S) combination.

METHODS: Patients (≥12 years) with moderate-to-severe persistent asthma previously treated with medium- to high-dose inhaled corticosteroids were randomized to twice-daily doses of either medium-dose MF/F (200/10 μg), medium-dose F/S (250/50 μg), high-dose MF/F (400/10 μg) or high-dose F/S (500/50 μg) for 1 year. The primary endpoint was the number and percent of patients reporting adverse events (AEs).

RESULTS: 404 patients were randomized (medium-dose MF/F, n = 141; high-dose MF/F, n = 130; medium-dose F/S, n = 68; high-dose F/S, n = 65). Medium and high MF/F combination doses were well tolerated and were associated with AEs of frequency and nature similar to AEs observed with F/S. The most common treatment-related AEs in the MF/F group were dysphonia (medium-dose MF/F, 5.0%, high-dose MF/F, 3.1%) and headache (medium-dose MF/F, 4.3%; high-dose MF/F, 3.1%); in the F/S group, headache (medium-dose F/S, 5.9% and high-dose F/S, 1.5%) and arthralgia (medium-dose F/S, 4.4%; high-dose F/S, 1.5%). Oral candidiasis was uncommon (MF/F overall, 1.1%; F/S overall, 2.2%). Six patients experienced serious AEs that were possibly drug-related; ocular changes (high-dose MF/F, n = 4; medium-dose F/S, n = 1); and pneumonia (medium-dose MF/F n = 1).

CONCLUSIONS: MF/F was well tolerated over 1 year at medium and high doses, with a safety profile similar to F/S and no unusual/unexpected AEs. Oral candidiasis was uncommon in this study.

607 Improvement of Bronchial Hypersensitivity and Non Asthma Attack Period of 3 months or more can Become A Stopping Criteria of Inhaled Corticosteroid in Child Asthma.

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RATIONALE: Prospective observation study aiming at finding out the criteria as the reducing and stopping of inhaled corticosteroids (ICSs) was performed in child asthma.

METHODS: It was targeted at 112 persons (average age 11.6+/-3.9) who have so far performed medical treatment with ICSs, and environmental management instruction by an allergy specialist. The patient did the step down of the ICSs (< fluticazone 100 mcg/day), and it checked that there was no asthma attack three months or more. Among them, 74 patients who by methacholine challenge test (MCT), PC20 stopped inhalation steroid by 74 persons of 0.5 mg/ml or more, and observed till 24 months. Among them, 74 patients of PC20 > 0.5 mg/ml by methacholine challenge test (MCT) stopped ICSs, and were observed for 24 months.

RESULTS: Fifty-five% of patients did not have a attack for 24 months. Per month, one or less asthma attack recurrence was 12%, and the dropout was 34%. There is no change of MCT in a non-asthma attack group, and there was aggravation of MCT in a attack recurrence group. There was no difference in a clinical index, a pulmonary function test, etc. by both groups.

CONCLUSIONS: If there is an improvement of the bronchial hypersensitivity more than fixed, 67% of patients controlled under suitable treatment can stop ICSs.

608 High Frequency of CF Transmembrane Conductance Regulator (CFTR) Mutations in a Population with Persistent Asthma and/or Chronic Rhinosinusitis

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RATIONALE: Cystic fibrosis (CF) is a common monogenic disease caused by mutations in the CFTR gene. Disease severity correlates with variable CFTR dysfunction caused by the type of mutation. CF varies by ethnic background, with 1:25 Caucasians estimated as carriers. Atypical (heterozygous) CF includes those with normal/borderline sweat chloride concentrations and pulmonary, GI, and/or rhinosinus disease. We hypothesize that full CFTR sequencing would reveal a large percentage of CF carriers in highly symptomatic patients.

METHODS: A retrospective chart review was conducted of pediatric and adult patients in the Divisions of Allergy/Immunology and Pediatric Pulmonology (n = 109) who had full CFTR genetic sequencing for the indications of persistent asthma, chronic rhinosinusitis (CRS) and nasal polyps. Symptoms and mutations known to effect CFTR function/phenotype were recorded and categorized per patient.

RESULTS:72 patients with asthma were identified, of which 28 (39%) had CFTR mutations. 38% (26/68) of patients with CRS, and 42% (16/38) of patients with both asthma and sinus disease had CFTR mutations. 4/6 patients (66%) with nasal polyps had CFTR mutations. 8 patients were found to have two CFTR mutations and 6 were empirically started on DNAse therapy. Genetic screening for the 23 most common CF mutations would have missed 30/41 carriers (73%).

CONCLUSIONS: The frequency of CF carriers (using full CFTR gene sequencing) is unknown. We suggest that there is a high CF carrier prevalence in patients with severe asthma, CRS and/or nasal polyps. The 23 mutation screen misses a significant percentage of these carriers, impacting disease management. Confirmation that these patients have a higher CF carrier frequency supports expanded full CFTR gene sequencing.

609 Clinical Implication of Sputum CXCL13 in Children with Asthma

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RATIONALE: CXCL13 is a chemokine which is known as a CXCR5 ligand, and also guides B lymphocytes to follicles in secondary lymphoid organs. IgE mediated allergic inflammation plays a key role in the pathogenesis of asthma, which brings to light the importance of IgE producing B lymphocyte. We investigated the clinical significance of sputum CXCL13 and its association with pulmonary function, bronchial hyperresponsiveness and eosinophilc inflammation in childhood asthma.

METHODS: We analyzed 160 children between 5 to 10 years of age. Pulmonary function tests and methacholine challenge tests were performed in all subjects. Blood eosinophil count, serum total IgE, serum eosinophil cationic protein (ECP) and sputum eosinophil count, ECP and CXCL13 were measured in all subjects.

RESULTS: There were 80 (54 male, 26 female;mean age, 8.3 ± 2.3 years) asthmatics and 80 (44 male, 36 female;mean age, 9.3 ± 2.5 years) controls. There were no differences in age and sex between the two groups. Asthmatic children had significantly higher levels of CXCL13 in induced sputum (112.01 ± 276.70 pg/mL) compared to healthy children (21.47 ± 25.18 pg/mL; P = .004). No associations were found between sputum CXCL13 and blood eosinophil count, sputum eosinophil count, serum ECP, sputum ECP, pulmonary function and bronchial hyperresponsiveness.

CONCLUSIONS: Our findings show that sputum CXCL13 may play a role in the pathogenesis of childhood asthma, independent of eosinophilic inflammation. Sputum CXCL13 could be one of the objective index in the diagnosis of asthma.