## 767 Low-dose Mometasone Furoate/Formoterol: Efficacy and Safety Findings from a Study Investigating a New Combination Therapy in Subjects Whose Asthma was Inadequately Controlled Using Low-Dose Inhaled Corticosteroid

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**RATIONALE:** Asthma is a variable disease. Optimal control in clinical practice often requires the use of therapy at varying doses. Availability of treatments at multiple strengths is therefore essential. These are results from a 6-month trial of a low-dose mometasone furoate/formoterol (MF/F) combination administered via MDI as treatment for exacerbations and bronchoconstriction in asthmatics previously treated with low-dose inhaled corticosteroids (ICS).

**METHODS:** In a randomized, multicenter, double-blind, placebo-controlled study in asthma subjects (≥12yrs) on low-dose ICS with/without LABA, subjects were assigned to 2-3 weeks of open-label MF 100mcg twice daily (BID), followed by 26 weeks of MF/F 100/10mcg, MF 100mcg, F 10mcg, or placebo (all BID). Co-primary endpoints were time-to-first severe asthma exacerbation to week 26 (MF/F versus F) and change from baseline to week 12 in serial FEV1 (0-12 hr); MF/F versus MF). Adverse events (AEs) were monitored.

**RESULTS:** 746 subjects (mean: age=38.3 years, asthma duration=14.77, FEV1% predicted=75.08, reversibility=18.69%, ACQ=1.31) were randomized. MF/F decreased the time-to and proportion of subjects experiencing severe exacerbations (MF/F=16.5%; MF=28.2% (p=0.006); F=44.7% (p<0.001); placebo=45.7% (p<0.001)). Rapid (<5 min) and sustained improvements in bronchodilation FEV1 (0-12 hr) were seen for MF/F vs MF (p=0.001) throughout the treatment period. These changes represented standardized increases in FEV1 from baseline ICS treatment of MF/F=13.8%, MF=9.0%, F=12.3%, and placebo=4.1% at week 12. Few AEs were observed and were similar between treatment arms.

**CONCLUSIONS:** In asthmatics inadequately controlled on low-dose ICS, MF/F 100/10mcg was more effective in reducing severe exacerbations and improving lung function than placebo, MF or F all administered by MDI.

## 768 Characterization of the Effect of Mometasone Furoate/Formoterol Treatment on Quality of Life: An Analysis of Multi-Trial AQLQ Findings

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**RATIONALE:** Clinical studies have shown that asthma reduces patients' quality of life. It is essential to properly characterize the effects that different strengths of mometasone furoate/formoterol (MF/F) MDI combination therapy have on QoL in subjects on low-, medium-, and high-dose ICS.

**METHODS:** The effect of MF/F treatment on asthma QoL was characterized in subjects who required low-(n=746), medium-(n=781), and high-dose ICS (n=728) maintenance treatments (monotherapy ± LABA). Data from 3 trials (all BID treatments) were studied: 1) low-dose MF/F (100/10mcg), low-dose MF (100mcg), F (10mcg), or placebo; 2) medium-dose MF/F (200/10mcg), medium-dose MF (200mcg), F (10mcg), or placebo; and 3) high-dose MF/F (400/10mcg), medium-dose MF/F (200/10mcg), or high-dose MF (400mcg). QoL changes were assessed using the standardized Asthma Quality of Life Questionnaire (AQLQ) for symptoms, activity limitation, emotional function, and environmental stimuli domains evaluated at baseline, Week 4, and endpoint (low- and medium-dose studies=week 26; high-dose study=week 12).

**RESULTS:** Baseline AQLQ-scores in the low-, medium-, and high-dose studies ranged between 5.55-5.71, 5.38-5.56, and 5.00-5.05, respectively. Clinically meaningful improvements (≥0.5) were observed across all MF/F doses investigated. Compared with placebo, MF/F treatment yielded statistically significant improvements at endpoint (MF/F 100/10mcg=0.42 vs -0.17; MF/F 200/10mcg=0.49 vs -0.01; MF/F 400/10mcg= not placebo compared) while MF or F monotherapy yielded smaller improvements (low/medium MF=0.34/0.37; F=0.02/0.05). In high-dose study, improvements at endpoint were 0.46 (high-dose MF/F) and 0.41 (high-dose MF).

**CONCLUSION:** Treatment with all doses of MF/F doses showed a clinically meaningful improvement in the AQLQ of asthma patients.

## 769 Efficacy and Safety of Medium and High Doses of Mometasone Furoate/Formoterol (MF/F) Combination Treatment in Subjects with Severe Persistent Asthma

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**RATIONALE:** Multiple strengths of mometasone furoate/formoterol (MF/F) MDI combination therapy are under investigation as new treatments for asthma. We report efficacy/safety findings from a 3-month MF/F study in subjects with severe asthma.

**METHODS:** This was a 3-month, randomized, double-blind, parallel-group, multicenter study with a 2-3-week open-label, run-in period of mometasone furoate (MF) 400mcg twice-daily (BID). Subjects (≥12 years) were randomized to MF/F (200/10mcg BID or 400/10mcg BID) or MF (400mcg BID). The primary endpoint was the area under the curve (AUC) of the change in serial FEV1 (0-12 hours) for MF/F 400mcg vs MF 400mcg from Baseline to Week 12. Adverse events (AEs) and other clinical safety measures were recorded.

**RESULTS:** A total of 728 subjects (mean: age 47.1 years, asthma duration 13.98 years, FEV1% predicted 66.31, reversibility 22.91%, Asthma Control Questionnaire (ACQ) Score 1.93) were randomized. Improvements in mean changes from baseline in FEV1 AUC (0-12 hours) at Week 12 were: MF/F 200/10mcg=3.59; MF/F 400/10mcg=4.19; MF 400mcg= 2.04 liters x hour, with both MF/F doses significantly better than MF (p<0.001). These FEV1s correspond to average hourly increases of 0.30, 0.35, and 0.17 liters, respectively. MF/F was associated with a rapid (<5 min) and sustained improvement in lung function. The percentage of subjects experiencing exacerbations was 12.4% (MF/F 200/10mcg), 12.2% (MF/F 400/10mcg), and 18.3% (MF 400mcg). There were no notable differences in AEs between the groups.

**CONCLUSIONS:** Both medium- and high-dose MF/F combination therapy led to significantly greater improvements in lung function compared with high-dose MF monotherapy in severe asthmatics.