

760 Asthma Symptom Control Using a Combination of Mometasone Furoate/Formoterol (MF/F): Grouped Analysis of Three Clinical Trials

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RATIONALE: The efficacy of asthma treatments is typically quantified using FEV1 which does not always correlate with asthma symptoms and quality of life. We characterized the ability of mometasone furoate/formoterol (MF/F) combination to improve asthma control in adults/adolescents inadequately controlled on low-, medium-, and high-dose ICS.

METHODS: Changes from baseline to endpoint in Asthma Control Questionnaire (ACQ) scores were assessed in subjects from 3 Phase III trials [low- (n=746), medium- (n=781), and high-dose (n=728)]. The ACQ categorizes asthma symptoms and use of rescue-medication using a 7-point scale (0=totally controlled, 6=severely uncontrolled). In the low- and medium-dose trials, subjects were randomized to receive MF/F (100/10mcg or 200/10mcg), MF (100mcg or 200mcg), F (10mcg), or placebo (26 weeks; all BID); In the high-dose trial, subjects were randomized to receive MF/F 200/10mcg, MF/F 400/10mcg, or MF 400mcg (12 weeks; all BID via MDI).

RESULTS: Baseline ACQ scores (1.23-1.38, 1.41-1.47, and 1.83-1.87 in the low-, medium-, and high-dose trial, respectively) indicated that subjects in all trials were not well controlled (<0.75) on ICS monotherapy. MF/F yielded ACQ improvements (100/10mcg=-0.36; 200/10mcg=-0.40) vs MF (100mcg=-0.26; 200mcg=-0.23), and deteriorations with F 10mcg (+0.07; +0.11) and placebo (+0.24; +0.14). MF/F 400/10mcg improved asthma control by -0.51 compared with -0.33 for MF 400mcg monotherapy. Improvements for MF/F at all doses achieved minimal importance difference of ≥ 0.5 point increase.

CONCLUSION: MF/F showed clinically important improvement in asthma control at all strengths and was better than MF, F and placebo.

761 Effect of Mometasone Furoate/Formoterol (MF/F) Combination Therapy on Nocturnal Awakenings in Subjects With Persistent Asthma

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RATIONALE: Asthmatics often report asthma-related nocturnal awakenings. These sleep interruptions may have significant impact in patients' quality of life. We characterized the effect of mometasone furoate/formoterol (MF/F) treatment on incidence of nocturnal awakenings requiring rescue-medication-use (SABA).

METHODS: MF/F's effect on nocturnal-awakenings requiring SABA was characterized across three Phase III efficacy trials (baseline=awakenings in week prior to first dose; endpoint=awakenings in last post-baseline Asthma-Control-Questionnaire result). Subjects were asthmatics previously treated with low- (n=746), medium- (n=781) or high-dose (n=728) ICS. Low-dose subjects were randomized to 26-weeks' treatment with MF/F 100/10mcg, MF 100mcg, F 10mcg, or placebo; medium-dose subjects to 26-weeks' treatment with MF/F 200/10mcg, MF 200mcg, F 10mcg, or placebo; high-dose subjects to 12-weeks' treatment with MF/F 400/10mcg, MF/F 200/10mcg, or MF 400mcg. All treatments were delivered twice-daily via MDI.

RESULTS: Baseline awakenings ranged from 0.84-1.05, 1.05-1.26, and 1.33-1.61 nights/week in the low-, medium-, and high-dose studies, respectively. In the low-dose study nocturnal awakenings were reduced by MF/F=-0.42, MF=-0.21, F=-0.21, and placebo=0.14 nights/week; corresponding changes in the medium-dose study were -0.56, -0.35, +0.07 and 0.00 night/week, respectively. In each of these placebo-controlled studies MF/F was superior to placebo (p<0.001) and F (p=0.035); MF was also superior to F and placebo. In the high-dose study, awakenings were reduced by -0.70, -0.70 and

-0.35 nights/week by medium-dose MFF, high-dose MF/F and high-dose MF, respectively; both MF/F treatments were superior to MF (p \leq 0.006).

CONCLUSION: Both MF/F and MF significantly reduced nocturnal-awakenings compared with F and placebo. Both doses of MF/F were superior to MF in the high-dose study.

762 The Particle Size of Mometasone Furoate 100 μ g and 200 μ g Dry Powder Formulations

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RATIONALE: Regional lung deposition of inhaled particles depends on particle size as well as inspiratory flow rate and other factors. Inhaled particles of aerodynamic size around 2 μ m have been found to deposit most efficiently in the alveolar region across a broad range of inspiratory flow rates. In vivo studies of mometasone furoate (MF) delivered by the Twisthaler[®] showed mean peak inspiratory flow rates (PIFR) at satisfactory levels in adult/adolescent patients aged ≥ 12 years (69 L/min), children aged 9-12 years (>60 L/min), and children aged 5-8 years (>50 L/min). We report particle size findings from an in vitro study analyzing the mass median aerodynamic diameter (MMAD) of MF.

METHODS: Twelve inhalers each of the 110 and 220 μ g/inhalation strengths were tested in vitro at the beginning and end of unit lives at a 60 L/min flow rate. Aerosolized MF was collected by cascade impaction for 2 inhalations from the 110 μ g/inhalation strength and 1 inhalation from the 220 μ g/inhalation strength, thereby providing similar particle masses.

RESULTS: The average MMAD of the 110 μ g strength for beginning and ending inhalations (n=24) was 2.0 μ m (range, 1.9-2.1 μ m), while the 220 μ g strength for beginning and ending inhalations (n=24) was 2.2 μ m (range, 2.0-2.4 μ m).

CONCLUSION: Average MMAD values of MF for both strengths measured in vitro at a clinically relevant flow rate, together with in vivo particle-size efficiency deposition models, suggest that the particle size of MF is optimal (~2 μ m) for efficient alveolar deposition when administered via the Twisthaler[®].

763 Effect of Treatment with Mometasone Furoate/Formoterol Combination (MF/F) on Rescue Medication Use

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RATIONALE: The use of rescue medication, such as short-acting β_2 -agonists (SABA), provides insight into disease control. We analyzed the effect of a new combination of mometasone furoate/formoterol (MF/F) on total daily use of SABA in subjects with asthma using data from two clinical trials

METHODS: Asthma subjects (≥ 12 years) previously treated with low-dose ICS (n=746) were randomized to 26 weeks twice-daily MDI treatment with MF/F (100/10mcg), MF (100mcg), F (10mcg) or placebo. In a second trial of identical design, 781 subjects previously treated with medium-dose ICS, were randomized to MF/F (200/10mcg), MF (200mcg), F (10mcg) or placebo. Using patient reported diary data, changes in mean AM/PM total rescue medication use (puffs + nebuliser) between baseline and endpoint were assessed.

RESULTS: In the low-dose trial, baseline use of rescue medication was: MF/F: 1.2, MF: 0.84, F: 1.14, and placebo: 1.03 daily puffs (+ nebulizer). Corresponding baseline use in the medium-dose trial were: MF/F: 2.02; MF: 1.64; F: 1.79; and placebo: 1.95. Changes in daily puffs of rescue medication in the low-dose trial were: MF/F (100/10mcg) = -53.4%; MF (100mcg) = -47.5%; F: +82.6%, and placebo: +47.5%. Changes in daily puffs of rescue medication in the medium-dose trial were: MF/F (200/10mcg) = -61.1%; MF (200mcg) = -22.1%; F: +184.1%, and placebo: +79.1%.

CONCLUSIONS: MF/F treatment reduced the use of rescue medication in subjects with persistent asthma previously treated with low- and medium-dose ICS monotherapy.