2. SYNOPSIS

Title of the Study: MOMETASONE FURONATE NASAL SPRAY VS. PLACEBO IN SUBJECTS WITH ALLERGIC RHINITIS AND COUGH (Protocol P01970)

Investigators: Multicenter

Study Centers: Multicenter: 11 centers in the UNITED STATES

Publication(s): None

Studied Period: 29 AUG 2000 to 06 DEC 2000

Clinical Phase: IV

Objectives: Primary: To compare between treatment groups the change in cough from Baseline to the end of the study.

Secondary: To compare between treatment groups the differences for the following: total nasal symptoms (sum of rhinorrhea, stuffiness/congestion, itching, sneezing), individual nasal symptoms, and response to therapy.

Methodology: This Phase IV, multicenter, randomized, double-blind, placebo-controlled, parallel-group study was conducted in conformance with Good Clinical Practices.

Number of Subjects: 245 subjects (83 men and 162 women), 12 to 74 years of age, were randomized at 11 study centers. 122 subjects were randomized to receive NASONEX Nasal Spray, and 123 subjects were randomized to receive placebo. 241 subjects completed the study, 245 subjects were included in the randomized population; 245 subjects were included in the safety population; 245 subjects were included in the intent-to-treat (ITT) population; and 224 subjects were included in the efficacy population.

Diagnosis and Criteria for Inclusion: Male and non-pregnant female subjects, 12 years of age or older, were eligible if they had a self-reported history of seasonal allergic rhinitis (SAR) with associated seasonal cough for at least 1 year and a positive skin test for a prevalent seasonal allergen (including seasonal molds); had a total nasal symptom score of at least 36 and a cough score of at least 5 for the 3 consecutive days prior to Baseline (Visit 3); and had completed the designated washout periods for all prohibited medications.

Subjects with pre-existing cough due to chronic bronchitis, chronic sinusitis, gastroesophageal reflux, asthma, medications such as angiotensin-converting enzyme (ACE) inhibitors, or conditions other than SAR were excluded. Also excluded were subjects who had upper or lower respiratory infections, subjects who were experiencing clinically relevant symptoms of wheezing, chest tightness, or shortness of breath, and subjects who were using breathed beta agonists more than twice per week (excluding pre-exercise).

Test Product, Dose, Mode of Administration, Batch Number: NASONEX Nasal Spray was supplied as a metered-dose. Subjects administered 2 actuations in each nostril once a day in the morning for a total dose of 200 ug/day. The batch number for NASONEX Nasal Spray was 76723-249.

Reference Therapy, Dose, Mode of Administration, Batch Number: Placebo was identical in appearance to the NASONEX active. Subjects administered 2 actuations in each nostril once a day in the morning. The batch number for placebo was 76723-042.

Duration of Treatment: Treatment was administered for 14 days.

Criteria for Evaluation:

Efficacy:

Primary: Between treatment group comparison of the change in cough from Baseline to the end of the study.

Secondary: Between group comparison of the changes in total nasal symptoms (sum of rhinorrhea, nasal stuffiness/congestion, nasal itching, and sneezing), individual nasal symptoms (based on a 4-point scale), overall nasal symptoms (sum of cough and total nasal symptoms) and response to therapy from Baseline to the end of the study based on a 5-point scale.
Title of the Study: MOMETASONE FURGATE NASAL SPRAY VS. PLACEBO IN SUBJECTS WITH ALLERGIC RHINITIS AND COUGH (Protocol P01970)

Safety: Adverse events (AEs)

Statistical Methods: All continuous variables were summarized using descriptive statistics (sample size, mean, standard deviation, median, and range) and analyzed using analysis of variance (ANOVA); all categorical measures were summarized using frequency and percentages and analyzed using a Cochran-Mantel-Haenszel (CMH) test. The hypotheses were tested at the α = 0.05 level using a 2-tailed test.

The primary efficacy variable was the change in cough from Baseline to the end of the study. Four separate null hypotheses were tested at three different times (AM, PM, and Daily Average); no treatment difference between the average week 1 changes from Baseline, no treatment difference between the average changes from Baseline of the last 7 non-missing days, and no treatment difference for all timepoints over both study weeks. Baseline was defined as the average of the 3 values (AM or PM) immediately prior to the Baseline visit. The AM, PM, and average daily values were tabulated and analyzed separately. The first three hypotheses were analyzed using a standard ANOVA (controlling for center, treatment and center by treatment interaction) and using a two-sided single degree of freedom F test gleaned from the PROC MIXED procedure in SAS®. The fourth hypothesis was tested using a longitudinal ANOVA and using a two-sided multi-degree of freedom F test gleaned from the PROC MIXED procedure in SAS®.

All secondary efficacy variables, except response to therapy, were analyzed using the same ANOVA model as was used in analyzing the primary efficacy variable. The 5-point Response to Therapy score was analyzed using the CMH test, stratifying by treatment group and center. A two-sided hypothesis of no difference in response to therapy for placebo versus Nasonex was tested using the CMH chi-square statistic. In cases where there was a treatment p-value at baseline that was ≤0.10, an ANCOVA was used to adjust for the treatment difference.

Adverse events (AEs) were coded using a WHOART dictionary, summarized by treatment group, and tabulated by overall subjects, WHOART Body System, and WHOART preferred term. The differences in the number of subjects reporting a treatment-emergent AE between the 2 treatment groups were compared using Fisher's Exact Test. AEs that were determined by the investigator to be related to the study drug (possibly, probably, or definitely related) were listed by the relationship; AEs were also listed by severity. Vital signs were summarized by treatment group.

SUMMARY - CONCLUSIONS:

Efficacy Conclusions:

For change from baseline of daytime cough (reflected in PM ratings), the Nasonex-treated group showed significant improvement at all timepoints and in the repeated measures analysis for the Efficacy population (p≤0.025), and at endpoint for the ITT population (p≤0.045). Change from baseline in nighttime cough (reflected in AM ratings) suggested advantages at all timepoints in favor of Nasonex over placebo in the ITT population; these differences did not reach significance (p>0.250). For the change from baseline of total nasal symptoms, the Nasonex-treated group (ITT and Efficacy) showed significantly greater improvement than placebo at all timepoints and variables (daytime and nighttime scores) compared to placebo (p≤0.035), with the exception of the Week 1 AM ratings. For overall symptoms (scoring total nasal), results for daytime symptoms showed significance in favor of Nasonex at all timepoints and in the repeated measures analysis (p≤0.011) for both ITT and Efficacy populations. Nighttime overall symptoms showed significance in favor of Nasonex at Week 2 and endpoint (p≤0.050) for the Efficacy population, and at endpoint (p=0.028) for the ITT population, with borderline significance both at Week 2 (p=0.051) and in the repeated measures analysis (p=0.052). Analysis of daytime individual nasal symptoms of congestion, nasal itching, and sneezing showed significant changes in favor of Nasonex for all timepoints (p≤0.021) and at endpoint for minimum (p≤0.038) for both the populations. The ITT analysis of nighttime nasal symptoms of congestion, nasal itching, and sneezing revealed significant changes from baseline in favor of Nasonex at all timepoints (p≤0.044), with the exception of congestion at Week 1. The therapeutic response analysis showed that twice as many Nasonex-treated subjects compared to placebo-treated subjects experienced "complete relief" or "marked relief" at Visit 4 (p≤0.027).

Safety Conclusions:

Overall, there were no significant differences in the safety profiles of Nasonex and placebo. The only SAE that occurred happened nearly 3 weeks after the subject (Nasonex) had completed study treatment, and it was not related to study drug.
Title of the Study: MOMETASONE FUMOATE NASAL SPRAY VS. PLACEBO IN SUBJECTS WITH ALLERGIC RHINITIS AND COUGH (Protocol P01970)

Overall Conclusion:
Nasonex is effective in the treatment of daytime cough associated with seasonal allergic rhinitis and in the treatment of nasal symptoms of SAR.

Date of the Report: 09 July 2001