Title of Study: Efficacy and Safety of SCH 29851 8 mg QD in Subjects With Seasonal Allergic Rhinitis (Protocol No. P00677)

Investigator(s): Multicenter

Study Center(s): 15 centers in the US

Publication(s): None

Studied Period: August 26, 1999 to November 10, 1999

Clinical Phase: III

Objective(s):

• The primary objective of this study was to assess the efficacy of SCH 29851 8 mg QD compared to placebo in subjects with seasonal allergic rhinitis.

• The secondary objective was to evaluate the safety profile of SCH 29851 using the following parameters: physical exam, subject and investigator reported adverse events, ECG, vital sign evaluations and laboratory results.

Methodology: Randomized, multicenter, double-blind, placebo-controlled, parallel groups.

Number of Subjects: Three hundred and sixty-two total, 130 men and 232 women, age 12-67 years; 182 subjects in the SCH 29851 8 mg QD group and 180 subjects in the placebo group.

Diagnosis and Criteria for Inclusion:

• Adult and adolescent subjects of either sex or any race, at least 12 years of age with a documented history of seasonal allergic rhinitis (SAR) for at least 2 years.

• Subjects must have a positive skin test (prick or intradermal) response to an appropriate seasonal allergen within the 12 months prior to the Screening visit.

• Subjects must be clinically symptomatic at the Screening visit with moderate scores for nasal rhinorrhea (at least 2), total nasal symptom score of at least 6, and total non-nasal score of at least 5.

• For 3 calendar days prior to Baseline, the 6 twice-daily run-in diary "reflective" scores were to total a minimum of 36 for the total nasal score, a minimum of 30 for the non-nasal score, and a minimum of 12 for the rhinorrhea score in order to qualify for randomization.

• Overall condition of seasonal allergic rhinitis was to be moderate or greater (score ≥2) at the Baseline visit.

• Subjects must be free of clinically significant disease, other than SAR.

• Female subjects of childbearing potential must have a negative serum pregnancy test (HCG) at Screening and must use a medically accepted method of birth control prior to Screening and during the study.

Test Product, Dose, Mode of Administration, Batch No(s): SCH 29851 8 mg tablet (Batch No. 0790088) to be administered orally once daily in the morning at approximately the same time each day.

Duration of Treatment: Two weeks.

Reference Therapy, Dose, Mode of Administration, Batch No(s): Placebo tablet (Batch No. 38101-098) to be administered orally once daily in the morning at approximately the same time each day.

Criteria for Evaluation: The primary efficacy variable was the mean change from Baseline in the average AM and PM reflective total symptom score from subject diaries. Secondary efficacy variables were to include mean change from Baseline in total symptom score minus congestion, nasal symptom score, nasal score minus congestion, and non-nasal symptom score.

Statistical Methods: The primary comparison was SCH 29851 8 mg QD vs. placebo, averaged over 15 days of treatment. After extracting sources of variability due to center and treatment, analysis of variance was used to analyze the responses for the primary and secondary variables for all treated subjects (ie, all randomized subjects that received at least one dose of study medication). Adverse events, vital signs, clinical laboratory tests and ECG evaluations were summarized by treatment group using descriptive statistics.
SUMMARY - CONCLUSIONS:

RESULTS:

Efficacy: The following conclusions on the efficacy of the SCH 29851 8 mg tablet can be drawn from this study:

- Treatment with SCH 29851 8 mg tablet resulted in a statistically significant reduction from Baseline compared to the placebo treatment group in the mean AM and PM (prior 12 hours) reflective total symptom score for seasonal allergic rhinitis for the primary time interval, Days 1-15, and all secondary time points.

- Supportive efficacy analyses using the evaluable subset of the ITT population confirmed the primary analysis that used an efficacy subset of the ITT population.

- All individual symptom scores, except for eye redness, were significantly reduced from Baseline for the primary time interval, Days 1-15, in the SCH 29851 treatment group compared to placebo.

- The evaluation of therapeutic response performed by the investigator showed statistically significant relief from the symptoms of seasonal allergic rhinitis over the primary time interval, Days 1-15, with SCH 29851 compared to placebo. There were no statistically significant differences in mean change from Baseline in the overall evaluation of seasonal allergic rhinitis between the two treatment groups.

Safety: The following safety conclusions can be drawn from this study:

- There were no unusual or unexpected adverse events with the SCH 29851 8 mg tablet and the pattern and incidence of adverse events, irrespective of relationship to study medication, was similar in the SCH 29851 and placebo treatment groups (59/182, 32.4% versus 56/180, 31.1%, respectively).

- The most common treatment-emergent adverse event, irrespective of relationship to study medication, reported in both treatment groups was headache (SCH 29851: 11/182, 6.0%; placebo: 14/180, 7.8%).

- Very few subjects experienced adverse events that were considered as possibly related to study medication (SCH 29851: 25/182, 13.7%; placebo: 20/180, 11.1%) and the majority in both treatment groups were rated as mild or moderate in severity. The most common possibly related adverse events reported in both treatment groups were dry mouth and headache. A greater number of subjects in the SCH 29851 treatment group experienced fatigue (6 subjects; 3.3%) compared to the placebo group (1 subject; 0.6%).

- There were no serious adverse events reported in this study.

- No clinically meaningful changes in clinical laboratory variables, vital signs, ECG parameters, or body weight were noted in either treatment group.

CONCLUSIONS:

- Treatment with SCH 29851 8 mg tablets resulted in a statistically and clinically meaningful improvement in the symptoms associated with seasonal allergic rhinitis for the total treatment period, Days 1-15. Overall, there were no clinically meaningful differences in safety or tolerability between SCH 29851 and placebo.

Date of the Report: July 7, 2000