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Proprietary Drug Name: NASACORT® AQ Nasal Spray	**INN:** Triamcinolone Acetonide Nasal Spray	**Therapeutic area and FDA approved indications:** For the treatment of nasal symptoms of seasonal and perennial allergic rhinitis in adults and children 6 years of age and older.

Name of Sponsor/Company:	Aventis Pharmaceuticals,Inc., Member of the sanofi-aventis group

Title of Study: (XRG5029C/4007). A Multicenter, Randomized, Single-Blind, Active-Controlled, Parallel Group Study Comparing the Efficacy of Nasacort® AQ Starting Dose of 220 mcg QD with Rhinocort Aqua™ Starting Dose of 64 mcg QD Given for One Week for the Treatment of Seasonal Allergic Rhinitis Symptoms in Subjects 12-65 Years of Age

Principal Study Investigators:

Study centres: Multicenter Study; 25 U.S. Sites

Publication:

Nayak A, Berger W, Liao Y, Garcia J, Georges G, and the Study 4007 Investigator Group. Tolerability and treatment response at starting doses of triamcinolone acetonide AQ and budesonide AQ in patients with seasonal allergic rhinitis. Abstract presentation at the Western Society of Allergy Asthma & Immunology January 2005. Kauai, Hawaii.

Study period (years): (date of first enrolment) (date of last completed): From12 February, 2003 to 10 June, 2003.	**Phase of development:** Phase IV

Objectives:

The primary objective of the study was to test the hypothesis that a significantly greater proportion of subjects would achieve ≥25% reduction from baseline in Total Nasal Symptom Score (TNSS) when started on Nasacort® AQ 220 mcg QD, compared with Rhinocort Aqua™ 64 mcg QD.

The secondary objectives of the study were to evaluate the following variables:

- proportion of subjects who achieve ≥25% reduction in mean changes from baseline in AM and PM TNSS
- proportion of subjects who achieve ≥20% and ≥30% reduction in mean change from baseline in TNSS
- individual nasal symptoms (nasal stuffiness, nasal discharge, sneezing, nasal itching) and eye symptoms for AM, PM, and daily (average of AM and PM scores) over the 1-week treatment period
- subjective subjects' and physicians' global evaluations of efficacy at the end of the 1-week treatment period.

Methodology:

Multicenter, randomized, single-blind, active-controlled, parallel group study. Subjects were to be randomized when spring pollen counts in the vicinity of the investigational sites had been elevated for at least 7 days prior to the randomization visit in order that subjects be exposed to grass or tree pollen and/or outdoor mold and be symptomatic during the 5 qualifying days prior to the visit. The presence of these allergens during the baseline period was to be obtained and recorded at the study site and furnished to the sponsor.

Number of patients (planned and analyzed):

A total of 450 subjects were planned to be enrolled.

A total of 618 subjects were screened.

- 476 Randomized
- 237 to Nasacort®AQ
- 239 to Rhinocort Aqua

A total of 470 subjects completed

- 233 Nasacort®AQ
- 237 Rhinocort Aqua

A total of 457 were protocol-correct

- 228 Nasacort®AQ
- 229 Rhinocort Aqua

Diagnosis and main criteria for inclusion:

Subjects included in the study were male or female, aged 12-65 years, who had at least a 2-year history of seasonal allergic rhinitis (SAR), met the minimum total nasal symptom score requirement of at least 42 out of 84, had a positive skin test to tree, grass pollen, and/or outdoor mold present in the subject's environment (documented historical testing performed during the past year was accepted), had no clinically significant abnormalities in physical examination or medical conditions that interfered with the study, had no oral/pharyngeal or nasal candidiasis, herpes, lesions, acute or chronic sinusitis, significant polyposis or deviated septum or other gross abnormalities of the nose, had not been recently exposed to rhinitis medications prior to randomization, and had no history of hypersensitivity to intranasal corticosteroids (INS) or their excipients.

Test product, dose and mode of administration, batch number:

Nasacort® AQ Nasal Spray, 2 sprays/nostril (55 mcg/spray) once daily for 7 ± 1 days. Lot number MN7001

Duration of treatment: 7 ± 1 days

Reference therapy, dose and mode of administration, batch number

Rhinocort Aqua™ Nasal Spray, 1 spray/nostril (32 mcg/spray) once daily for 7 ± 1 days. Lot number DC 272

Criteria for evaluation:

Efficacy:
Primary efficacy data were the proportion of subjects who achieved ≥25% reduction in mean change from baseline in daily TNSS (sum of scores for nasal stuffiness, nasal discharge, sneezing, and nasal itching). Symptom scores were recorded twice daily (AM and PM) and scored numerically on a scale of 0 (symptom absent) through 3 (severe).

Secondary efficacy data were the proportion of subjects who achieved ≥25% reduction in mean changes from baseline in AM (upon arising in the morning before study medication) and PM (before bedtime) TNSS; the proportion of subjects who achieved ≥20% and ≥30% reduction in mean change from baseline in TNSS; the mean daily individual nasal symptom scores (nasal stuffiness, nasal discharge, sneezing, nasal itching) and total eye symptom scores (itchiness, tearing, redness) for AM, PM, and daily (average of AM and PM scores) over the 1- week treatment period; and the subjective subjects' and physicians' global evaluations of efficacy at the end of the 1- week treatment period.

Safety:
Safety was assessed on the basis of clinical examination findings and reports of adverse events (AE).

Statistical methods:

The proportion of subjects who achieved ≥25% reduction in mean change from baseline in daily TNSS was compared between 2 treatment groups using Chi-square test at a 2-sided, 0.05 significance level.

For each nasal/ocular symptom variable (AM, PM, and daily average of AM and PM scores) and each subject, a mean change from baseline score was calculated for the 1- week treatment period. The mean baseline daily TNSS and eye symptoms values were calculated using the 3 baseline daily total nasal and ocular symptoms scores, respectively, immediately preceding Visit 2 (randomization). The mean change from baseline variables were analyzed using ANCOVA models that included treatment, center effects, and baseline scores.

Subjects' and physicians' global evaluations of efficacy were analyzed in 2 ways. First, the data was presented in contingency tables and treatment effect was compared using

Chi-square/Fischer's exact test and Cochran-Mantel-Haenszel (CMH) test. Second, the evaluation score was treated as a continuous variable and simple summary statistics (mean, standard variance, range) were calculated.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

% Subjects with ³25% reduction in TNSS: There was no statistically significant difference between Nasacort® AQ and Rhinocort Aqua™ in the proportion of subjects who achieved a 25% or greater reduction from baseline in TNSS (*P*>0.7). The percentage of subjects who achieved a 25% or greater reduction from baseline in TNSS at 1 week of treatment was 58.6% for Nasacort AQ® and 61.9% for Rhinocort Aqua™.

The results for the secondary efficacy variables: proportion of subjects who achieved a ≥25% reduction from baseline in morning and evening TNSS and the proportion of subjects who achieved ≥20% and ≥30% reduction from baseline in TNSS, are presented in the table below. The results were consistent with those from the primary endpoint. There were no significant differences between the Nasacort® AQ and Rhinocort Aqua™ groups for any of these secondary efficacy variables (*P*>0.3).

Baseline Symptom Scores: Mean baseline scores in both treatment groups were approximately 2 (moderate) for each of the individual symptoms. There were no statistically significant differences between Nasacort®AQ and Rhinocort Aqua™ in the reduction of symptoms from baseline of the individual nasal symptoms, total eye symptoms, and TNSS (*P*>0.4).

Physicians (who were blinded to the treatment assignment) assessed efficacy of treatment on a 5-point scale from 0 (no relief) to 4 (complete relief) after 1 week of treatment.

% Subjects with Moderate-Complete Relief: The percentage of subjects who had moderate to complete relief of symptoms, as rated by physicians was 65.6% for the Rhinocort Aqua™ group and 59.1% for the Nasacort® AQ group. There was no statistically significant difference between Nasacort® AQ and Rhinocort Aqua™ for the overall physician global assessment of efficacy (*P*>0.4)

Global Assessment of Efficacy: The global assessment of efficacy by the subjects was comparable to that of the physicians. The percentage of subjects who had moderate to complete relief of symptoms was 67.8% for the Rhinocort Aqua™ group and 64.4% for the Nasacort® AQ group. There was no significant difference between Nasacort® AQ and Rhinocort Aqua™ in the global assessment of overall treatment efficacy by the subjects (*P*>0.3).

SAFETY RESULTS:

There was no significant difference between treatment groups in the mean number of days of exposure to study medication. The proportion of subjects in each treatment group who experienced an AE was comparable: 11.77% of the Rhinocort Aqua™ group and 12.7% of the Nasacort® AQ group. The most commonly occurring treatment-emergent adverse events (TEAEs) were classified in the respiratory, thoracic, and mediastinal body system (3.2%). All other TEAES were experienced by fewer than 3% of the subjects. In the Rhinocort Aqua™ treatment group, 6 of the 28 AEs were assessed by investigators as being possibly related to study medication. Two of the events were assessed as severe, 10 as moderate, and 16 as mild.

Similarly, 8 of the 30 AEs in the Nasacort® AQ group were assessed as being possibly related to study medication. Five of the events were assessed as severe, 8 as moderate, and 17 as mild.

Three Nasacort® AQ –treated subjects w ere discontinued from the study due to AEs. None of these events were assessed by investigators as being related to study medication. Two of the subjects developed sinus infections and the other subject developed a severe upper respiratory infection. None of the Rhinocort Aqua™-treated subjects were discontinued from the study due to an AE.

No deaths occurred during the study and there was only 1 event assessed by an investigator as a serious adverse event (SAE): hospitalization for repair of a wound of the upper thigh following a fall.

Date of the report: 28 February, 2004