**CLINICAL STUDY SYNOPSIS**

*(Final)*

**Title of the study:** A DOUBLE-BLIND COMPARISON OF Budesonide Dry Powder AND PLACEBO IN THE TREATMENT OF CHILDREN WITH PERENNIAL ALLERGIC RHINITIS

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**Study site(s):** Five centres in USA.

**Publication (reference):** -

**Study period:** The first patient was enrolled on 12 December 1991 and the last patient completed the study on 10 November 1992.

**Clinical phase:** III

**Objectives:**

1. To determine the efficacy and safety of once-daily dosing of 200 µg and 400 µg of budesonide, administered via Turbuhaler®, as compared to placebo during a six-week treatment period in children with perennial allergic rhinitis.

2. To evaluate the safety and tolerability of once-daily dosing of budesonide, administered via Turbuhaler®, during a six-month open-label treatment period.

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Study design: The protocol was designed as a six week double-blind, randomized, placebo-controlled, parallel-group multicenter study in children with perennial allergic rhinitis. A six-months open label period followed the double-blind period.

Number of patients (total and for each treatment): Thirty-nine patients received placebo, while 38 patients each received budesonide 200 µg OD and 400 µg OD, respectively.

Diagnosis: Perennial allergic rhinitis.

Criteria for inclusion:
1. Patients, males or females aged 6 to 18 years, with a clinical diagnosis of perennial allergic rhinitis for at least one year and had given written informed consent.
2. Patients with at least two of the symptoms of blocked nose, runny nose or sneezing with severity scores greater than or equal to 1 (mild symptoms) during at least 3 days of a one-week baseline period.

Criteria for exclusion:
1. Patients with seasonal allergic rhinitis to allergens occurring during the double-blind part of the study period or patients with a significant upper respiratory tract infection in the two weeks prior to enrolment.
2. Patients with infectious rhinitis/sinusitis/otitis, rhinitis medicamentosa, atrophic rhinitis, nasal polyposis, structural nasal abnormalities severe enough to cause obstruction.
3. Patients who required asthma treatment with inhaled or systemic corticosteroids or on maintenance immunotherapy not on constant level throughout the study.

Investigational drug: Budesonide, Rhinocort® Turbuhaler® 200µg/ dose, Batch DRK 62
Budesonide, Rhinocort® Turbuhaler® 100µg/ dose, Batch DRI 63.

Reference treatment(s): Placebo for Rhinocort Turbuhaler®, Batch DRI 64.

Duration of treatment: Randomized double blind treatment during six weeks followed by open-label treatment during six months.

Assessment methods:
Efficacy was assessed by evaluation of rhinitis symptom scores, use of concomitant medication recorded in the diaries and patient's global assessment of response. Safety was assessed in terms of adverse events, physical examinations and laboratory evaluations. Morning basal plasma cortisol level and iv post ACTH stimulation (Cortrosyn®) plasma cortisol level were determined as screening, at the end of double-blind treatment and at the end of open-label treatment.

Statistical methods:
The primary efficacy variables were the three nasal symptom scores. The change from baseline in the mean values of symptom scores (during double-blind period) were subjected to analyses of covariance followed by pairwise comparisons. The same analyses was done during the open label period. The global assessment of treatment efficacy was analysed using Cochran-Mantel-Haenszel statistic. The change of laboratory assessments from baseline were

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subjected to analyses of covariance followed by pairwise comparisons. Results were reported as statistically significant if a two-sided test p-value of 0.05 or less was attained.

Summary of results:

The double-blind period.
One-hundred fifteen patients entered the double-blind part of the study. Ages of all patients were between 6 and 19 years with mean ages ranging from 12.9 to 13.5 years in the three groups. Seventy-one to 77% in each treatment group were males. The individual nasal symptom scores (blocked nose, runny nose, sneezing, and combined nasal score) showed no statistically significant differences between the budesonide groups and the placebo group. The global self-assessment score indicated greater control over perennial allergic rhinitis symptoms in patients treated with budesonide as compared to placebo, although pairwise differences between the treatments did not achieve statistical significance (p > 0.078). Neither budesonide dose group showed significantly greater improvement in eye symptoms than the placebo group. Neither budesonide dose group showed significantly lower usage of rescue medication in the treatment period than the placebo group. No serious adverse events occurred. A similar number of patients in each group discontinued double-blind therapy. The overall incidence of adverse events during the double-blind treatment period was comparable among the three treatment groups. As measured by both basal and stimulated cortisol values, budesonide had no suppressive effect in this study on hypothalamic-pituitary-adrenal axis.

The open label period.
Sixty-one patients entered the open-label period and fifty-one of them completed the six months treatment. The placebo group experienced a decrease in the morning and evening nasal symptom scores (indicating improvement) once they began taking budesonide 400 μg OD and the reductions from pre double-blind baseline were somewhat larger than those experienced by the patients who were on active drug during the double-blind period. The eye symptom scores closely resembled the results for the primary efficacy variables. The patients who received placebo during the double-blind period reported having more control over their symptoms than those receiving budesonide during the double-blind period. There was virtually no use of rescue medication recorded in the patient diaries for the open-label period. No abnormal changes were detected during nasal examinations. Few laboratory values were outside predefined limits, most were in the placebo group, and none represented clinically significant events. The mean corticotropin (Cortrosyn®) stimulated plasma cortisol levels and mean changes from baseline were similar among the groups in the open-label period. The overall incidence of adverse events during the double-blind treatment period was comparable among the three treatment groups.

Conclusions:
Results of this randomized, parallel-group, placebo-controlled study fail to demonstrate that once-daily budesonide (200 or 400 μg) provides a statistically significant benefit in alleviating symptoms associated with mild perennial allergic rhinitis in children during a six-week double-blind treatment period. Some efficacy activity was evident on the basis of trend in global assessment scores, but this benefit was not supported by improvement in individual nasal symptoms. The profiles of adverse experiences and laboratory variables were similar for both budesonide-treated and placebo-treated patients; budesonide appeared to be well tolerated.

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