CLINICAL STUDY SYNOPSIS

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<tr>
<th>NAME OF COMPANY:</th>
<th>AB Draco (a subsidiary of AB Astra), Lund, Sweden</th>
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<tr>
<td>TRADE NAME:</td>
<td>Rhinocort® Turbuhaler</td>
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<tr>
<td>NAME OF ACTIVE INGREDIENT INN:</td>
<td>Budesonide</td>
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| (FOR NATIONAL AUTHORITY USE ONLY) |

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<tr>
<th>STUDY CODE:</th>
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<td>005-2172</td>
<td>850-CR-2135</td>
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Title of the study: A comparison of the efficacy and tolerability of budesonide given intranasally as a dry powder (via Turbuhaler®) to placebo in children with seasonal allergic rhinitis

Investigator: Day JH

Study centre: Kingston General Hospital, Division of Allergy, Kingston, Ontario, K7L 2V7 Canada

Publication (reference):

Study period: August 1990 - October 1990

Clinical phase: III

Objectives: To compare the efficacy and tolerability of budesonide given intranasally as a dry powder with that of placebo in the treatment of seasonal allergic rhinitis.

Study design: Double-blind, randomized, parallel. One-week baseline period followed by a 3-week treatment period.

Number of patients (total and for each treatment): A total of ninety-seven, fifty-seven boys and forty girls aged 6-18. There were thirty-two in the budesonide 400 µg group, thirty-three in the budesonide 200 µg group and thirty-two in the placebo group.

Diagnosis and criteria for inclusion: Ragweed-induced seasonal allergic rhinitis of at least one year's duration. Ragweed sensitivity was verified by provocation. Age 6-18.

Investigational drugs, dose and mode of administration, batch No.: Rhinocort® Turbuhaler, batches Nos DQG 43 and DQG 44, supplied in powder inhalers containing 200 doses of budesonide and delivering either 100 µg or 200 µg per actuation. The dosage was one actuation in each nostril in the morning.

Reference drugs, dose and mode of administration, batch No.: Placebo for Rhinocort Turbuhaler, batch No DQG 45.

Duration of treatment: Three weeks.

Assessment methods: Throughout the study the patients scored on a 4-point scale the severity of the

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symptoms experienced in the preceding 24 hours. At the conclusion of each period the patients made
an overall assessment of the trial medication. Rhinoscopy was made at entry and after the treatment
period. Laboratory measurements (haematology, blood chemistry, urinalysis) were made before and
after the study.

Statistical methods: The mean values of the symptom scores for the individual symptoms and eye
symptoms as well as a mean combined score for nasal symptoms over the 3-week treatment period were
calculated. The change in these mean scores from baseline was subjected to ANOVA based on ranked
scores.

The change in weekly consumption of terfenadine from baseline was compared between treatments
using an ANOVA on ranked scores.

Global assessment of treatment efficacy (at the end of the study) and compliance using ranked scores
was analyzed with ANOVA.

The change in rhinoscopy findings and the urinary cortisol and creatinine levels from visit 1 to visit 3
was analyzed with Wilcoxon signed rank test. The comparison in these changes between treatments
was accomplished by using ANOVA on ranked scores.

All other laboratory assessments were analyzed with respect to the change from baseline (visit 1) to
visit 3 by Wilcoxon’s signed rank test.

I all tests using ANOVA mentioned above pairwise comparisons of treatments were accomplished.

All tabulations were produced by a Tabulate procedure in the statistical package SAS (ver. 6.08 under
VAX/VMS). The same program was used for all statistical analyses. Figures were produced using SAS
Graph.

Summary of results: Ninety-seven subjects, fifty-seven boys and 40 girls aged 6-18, entered the study
and all of them completed the study. Thirty-two subjects received 400 µg budesonide/day, thirty-three
received 200 µg and thirty-two received placebo. The symptoms showed significant improvement in
both budesonide groups, whereas in the placebo group there were only non-significant changes
compared with baseline. Approximately half the patients in the budesonide groups stated that they had
achieved total or substantial control over symptoms whereas the corresponding figure for the placebo
group was only 22%. The rhinoscopic examinations also indicated improvement of most of the signs
though there was no significant difference between the groups. There were reductions in urine cortisol
in all groups but there was no statistically significant difference between the groups. There were minor
non-significant reductions in creatinine in the 400 µg and the placebo groups and a significant
reduction in the 200 µg groups but, again, there was no statistically significant difference between the
groups. The adverse reactions were generally mild and transient. The most frequent reactions were
rhinitis, coughing, pharyngitis and headache. Headache was more frequent during treatment with 400
µg than 200 µg but there was no difference when either dose was compared with placebo. There was
no serious adverse event.

Conclusion: The results show that Rhinocort® Turbuhaler® is effective and safe in the treatment of
children with seasonal allergic rhinitis, whether given in the dosage 200 µg or 400 µg daily.

Date: July 31, 1992

Author: Lars-Erik Richard

Statistician: Lars Ek

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