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CLINICAL STUDY REPORT

DRUG SUBSTANCE	Budesonide
DOCUMENT NO.	SD-005-CR-0341
VERSION NO.	1
STUDY CODE	SD-005-0341
DATE	30 March, 2000

FINAL

A study assessing efficacy of budesonide aqueous nasal spray (Rhinocort® Aqua) in children with perennial allergic rhinitis

STUDY PERIOD:	15 November 1997 - 19 April 1999
PHASE OF DEVELOPMENT:	IIIB
STUDY DESIGN:	Double-blind, placebo-contolled, randomized, parallel group
DIAGNOSIS:	Perennial allergic rhinitis
TEST DRUG AND DOSAGE:	Budesonide aqueous nasal spray (Rhinocort® Aqua) 128 μg
COMPARATOR DRUG AND DOSAGE:	Placebo
DURATION OF TREATMENT:	6 weeks

The study was conducted in accordance with the principles of Good Clinical Practice.

INVESTIGATOR SIGNATORY:

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DRUG PRODUCT	Rhinocort® Aqua	**Synopsis**	(FOR NATIONAL AUTHORITY USE ONLY)
DRUG SUBSTANCE(S)	Budesonide	REFERRING TO PART OF THE DOSSIER	
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A study assessing efficacy of budesonide aqueous nasal spray (Rhinocort® Aqua) in children with perennial allergic rhinitis

INVESTIGATOR

W.J. Fokkens, Erasmus University Rotterdam 3015 GD ROTTERDAM, Holland

STUDY CENTRES

Multicentre, multinational study: 25 centres in Holland, 7 centres in Hungary and 3 centres in Portugal.

PUBLICATION (REFERENCE)

STUDY PERIOD		**PHASE OF DEVELOPMENT**
- **DATE OF FIRST PATIENT ENROLLED**	15 November 1997	IIIB
- **DATE OF LAST PATIENT COMPLETED**	19 April 1999	

OBJECTIVES

Primarily to demonstrate the efficacy of budesonide aqueous nasal spray in children with perennial allergic rhinitis.

Secondarily to study the ability of different efficacy variables to demonstrate the efficacy and to evaluate the general tolerability of investigational procedures and investigational drugs

STUDY DESIGN

The study was of a double-blind, placebo-contolled, randomized, parallel group design

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION/EXCLUSION

The diagnosis was perennial allergic rhinitis for at least one year.

Tha main inclusion criteria were: out-patients, 6-16 years of age, with moderate to severe nasal symptoms.

The main exclusion criteria were: patients with tree or grass pollen allergy in season, upper respiratory infection within 2 weeks before visit 1, rhinitis medicamentosa, structural abnormalities of the nose, and systemic corticosteroid treatment within two months before visit 1.

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

The test product was budesonide aqueous nasal spray (Rhinocort® Aqua), administered intranasally once daily in the morning with 1 spray in each nostril.

Test product	Strength	Batch number
Budesonide aqueous nasal spray	1.28 mg/mL containing 120 doses of 64 μg budesonide	YD 51

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

The comparator product was placebo aqueous spray identical in appearance to the test product, administered intranasally once daily in the morning with 1 spray in each nostril. The batch number of placebo aqueous spray was YE 21.

DURATION OF TREATMENT

The treatment was given once daily in the morning for 6 weeks.

MAIN VARIABLE(S):

- **EFFICACY**

Primary efficacy variables were the combined nasal symptom score (the sum of blocked nose, runny nose and sneezing) and values of PNIF measurements from the childrens' diaries.

The secondary efficacy variables were the nasal symptoms recorded at home both on a visual analogue scale and scored from 0 to 3 by the child and one parent in separate diaries, Quality of Life (only in Holland), overall evaluation of treatment efficacy by both the child and one parent and nasal cytology (eosinophils) for a sub-group of patients.

- **SAFETY**

Registration of adverse events.

STATISTICAL METHODS

The mean values for the combined and individual nasal symptom scores, PNIF were calculated for the last week during the run-in period (baseline) and the two last weeks during the treatment period. As endpoint for the statistical analysis using ANOVA (with

treatment and country included in the model) the change from baseline was used. The baseline mean score was included in the model as a covariate.

The change of the percentage of eosinophils from baseline (visit 2) was subjected to a non-parametric test (Wilcoxon). For Quality of Life parameters the change from visit 2 to visit 4 was calculated and analysed. Overall evaluation of treatment efficacy was analysed using an ANOVA model with treatment and country as included factors. Evaluation of each investigational procedure was analysed by means of descriptive statistics.

A post-hoc analysis was performed concerning onset of action of BANS using ANOVA with treatment and country included in the model.

PATIENTS

	BANS	**Placebo**	**Total**
No. planned	100	100	200
No. randomized and treated	100	102	202
Males/ Females	72/ 28	67/ 35	139/ 63
Mean age (range)	10.5 (6-16)	10.7 (6-16)	10.6 (6-16)
No. analysed for efficacy	100	102	202
No. analysed for safety	100	102	202
No. completed	94	98	192

SUMMARY - CONCLUSION(S)

- **EFFICACY RESULTS**

Primary variables

Budesonide aqueous nasal spray (BANS) improved the combined and the individual nasal symptom scores and peak nasal inspiratory flow significantly more than placebo. The reduction after 6 weeks of treatment of the combined nasal symptom score in the evening was 1.86 in the BANS group and 0.93 in the placebo group ($p<0.001$).

Peak nasal inspiratory flow increased 35.8 L/min in the BANS treated patients and 11.4 L/ min in the placebo treated patients after 6 weeks ($p<0.001$).

Secondary variables

BANS treated patients were significantly more improved than placebo for the combined nasal symptom score irrespective if the scoring was done by the child or the parent, in the morning or evening, or using the scoring from 0 to 3 or VAS scoring. The three individual

nasal symptoms (blocked nose, runny nose and sneezing) were significantly more improved in the BANS treated patients.

Quality of life data were available for a subset of patients in Holland. There was a numerical though not significant difference between the treatment groups (p=0.19).

With regards to the patients' overall evaluation of treatment efficacy, patients receiving BANS rated efficacy higher than did patients receiving placebo (p<0.001).

Nasal cytology was performed for a sub-group of patients in Holland. The number of eosinophils decreased in the BANS group while there was a slight increase in the placebo group (p=0.011).

All investigational procedures were rated acceptable (rated at least quite well) by the majority of patients except for the cytology cell sampling.

Onset of action for BANS in children was 12 hours after first dose for combined nasal symptom scores and 48 hours for PNIF.

- **SAFETY RESULTS**

The number, nature and intensity of the adverse events was similar in both treatment groups.

DATE OF THE REPORT

30 March 2000