Clinical Pharmacology Study Report

Drug Substance	Rhinocort Aqua
Study Code	SD-005-0689
Date	10 July 2007

A comparison of the nasal mucosal tissue concentrations of budesonide, budesonide oleate, budesonide palmitate and mometasone furoate in seasonal allergic rhinitis patients out of season

Study dates:	First subject enrolled:	29 March 2001
	Last subject completed:	29 April 2001
Phase of development:	Clinical Pharmacology (I)	

This study was performed in compliance with Good Clinical Practice

Drug Substance(s)	Rhinocort Aqua	**SYNOPSIS**	(For national authority use only)
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A comparison of the nasal mucosal tissue concentrations of budesonide, budesonide oleate, budesonide palmitate and mometasone furoate in seasonal allergic rhinitis patients out of season

Study centre(s)

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Study dates		**Phase of development**
First subject enrolled	29 March 2001	Clinical pharmacology (I)
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Objectives

The primary objective was to compare the tissue concentrations of budesonide (Bud) with the tissue concentrations of mometasone furoate (MF) after concomitant administration of 256 µg budesonide and 200 µg MF aqueous nasal sprays.

The secondary objective was to look at the budesonide palmitate (BP) and budesonide oleate (BO) ester concentrations at the different time points after drug administration.

Study design

The study was of an open, randomized design involving four study visits. The patients were randomized into 4 groups of 8 patients. Each patient concomitantly administered single doses of budesonide and MF on one occasion. Drug administrations took place at the clinic in the morning.

After administration of both drugs, two nasal biopsies, one from each nostril and time point were taken from each patient as follows:

- Group 1, at 2 and 6 hours after drug administration

- Group 2, at 6 and 12 hours after drug administration

- Group 3, at 2 and 12 hours after drug administration

- Group 4, before and at 24 hours after drug administration

Group 4 had the “before biopsies” taken within 5 to 10 days before drug administration, this to allow healing of the nasal mucosa prior to drug administration.

Target subject population and sample size

Patients with seasonal allergic rhinitis (SAR). N=32

Investigational product and comparator(s): dosage, mode of administration and batch numbers

The following doses were administered:

- 256 µg budesonide, 4 sprays of 64 µg (2 sprays per nostril) via Rhinocort Aqua Nasal Spray, Batch 8102 AK81

- 200 µg mometasone furoate, 4 sprays of 50 µg (2 sprays per nostril) via Nasonex Nasal Spray, Batch 00L0879.

- 0 µg placebo, 4 sprays (2 sprays per nostril) for Rhinocort Aqua Nasal Spray, Batch 2902 AK29

Duration of treatment

Single dose.

Variables

- **Pharmacokinetic**

  Concentrations of budesonide, budesonide oleate, budesonide palmitate, and mometasone furoate in nasal biopsy samples.

- **Pharmacodynamic**

  Not applicable

- **Pharmacogenetics**

  Not applicable

- **Safety**

  Reports of serious adverse events (SAEs) and discontinuations due to adverse events (DAEs)

Statistical methods

All hypothesis testing was done using two-sided alternative hypotheses. P-values less than 5% were considered statistically significant.

Student's t-test was used to compare (1) the concentrations of budesonide alone with the concentrations of mometasone furoate and (2) the combined concentrations of budesonide and its two esters with the concentrations of mometasone furoate. The comparisons were made in three ways: (1) using the actual concentration data; (2) after adjusting the concentrations for the differences in given drug weights; and (3) after adjusting the concentrations for the differences in number of moles of drug.

Subject population

Of the 32 patients allocated to treatment, 17 (53.1%) were males and 15 (46.9%) were females. Their average age was 30.5 years (range: 18–51). All were Caucasian.

Summary of pharmacokinetic results

Table S1 shows statistical comparisons between the concentrations of budesonide alone or together with its esters and that of mometasone furoate.

Table S1 Comparisons of concentrations

Time	Contrast	Ratio	95% confidence interval	P-value
2 h	Bud vs. MF	5.23	(2.41, 11.35)	0.0005
	Total-bud vs. MF	11.46	(5.43, 24.19)	0.0000
6 h	Bud vs. MF	2.45	(1.46, 4.12)	0.0025
	Total-bud vs. MF	4.52	(2.74, 7.44)	0.0000
12 h	Bud vs. MF	0.91	(0.54, 1.55)	0.7185
	Total-bud vs. MF	1.53	(0.95, 2.47)	0.0742
24 h	Bud vs. MF	0.29	(0.11, 0.79)	0.0233
	Total-bud vs. MF	0.77	(0.34, 1.76)	0.4701

The concentrations of budesonide (with and without its esters) are significantly higher than those of mometasone furoate after 2 and 6 hours. Very few samples for mometasone furoate and budesonide palmitate had detectable concentrations at 12 and 24 hours.

Summary of pharmacodynamic results

Not applicable

Summary of pharmacokinetic/pharmacodynamic correlations

Not applicable

Summary of population pharmacokinetics

Not applicable

Summary of pharmacogenetics

Not applicable

Summary of safety results

There were no serious adverse events reported during this study (only safety variable collected).

1. REFERENCE LIST

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