Pharmacokinetics of budesonide controlled ileal release capsules in children and adults with Crohn's disease

STUDIED PERIOD: June 24, 1996 – May 22, 2001
PHASE OF DEVELOPMENT: I
STUDY DESIGN: Open
DIAGNOSIS: Active Crohn’s disease
TEST DRUG AND DOSAGE: Budesonide Controlled Ileal Release (CIR) capsules 9 mg dosed in the morning.
Budesonide solution for intravenous infusion 0.5 mg.
COMPARATOR DRUG AND DOSAGE(S): -
DURATION OF TREATMENT: Budesonide CIR capsules for seven days, single intravenous infusion.

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

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SPONSOR’S SIGNATORY:
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### Synopsis

**NAME OF SPONSOR/COMPANY**
AstraZeneca R&D Lund

**NAME OF FINISHED PRODUCT**
Entocort® Capsules

**NAME OF ACTIVE INGREDIENT**
Budesonide

**STUDY CODE**
08-3044

**VOLUME FINAL REPORT NO.**
08-CR-3044

**DATE OF FIRST ENROLMENT**
1996 06 24

**DATE OF LAST COMPLETED**
2001 05 22

**PHASE OF DEVELOPMENT**
I

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**TITLE OF THE REPORT**
Pharmacokinetics of budesonide controlled ileal release capsules in children and adults with Crohn's disease

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**STUDIED PERIOD**
- **DATE OF FIRST ENROLMENT**
  1996 06 24
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**OBJECTIVES**
The primary aim was to evaluate the rate and extent of systemic availability of budesonide in children with Crohn’s disease (CD) and compare the results with those in adults with CD after
administration of budesonide Controlled Ileal Release (CIR) capsules. The secondary aim was to study the systemic effects, measured as plasma cortisol levels and compare the results from the children with those from the adults.

STUDY DESIGN
Open.

NUMBER OF PATIENTS (PLANNED AND ANALYSED)
Eight children and eight adults were planned. Results from eight children (mean age 12 years) and six adults (mean age 33 years) are presented in this report.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION
A diagnosis of Crohn’s disease, at least in the ileum and/or ascending colon. Active Crohn’s disease, i.e. PCDAI ≥ 25 or CDAI ≥ 150 (children 6-14 years) and CDAI ≥ 200 (adults 18-70 years).

TEST DRUG, DOSAGE AND MODE OF ADMINISTRATION, BATCH NUMBER
Budesonide CIR capsules; 9 mg orally dosed in the morning:
Budesonide solution for intravenous infusion 25 µg/mL - 20 mL (dose 0.5 mg):
batch DXD 17 (patient No. 101), batch DXH 20 (patient Nos. 102-103), batch DYB 22 (patient Nos. 104, 501-504 and 701), batch DZA 23/1 (patient No. 702).

DURATION OF TREATMENT
Budesonide CIR capsules for seven days, single budesonide intravenous infusion (only to 4 children and 6 adults).

MAIN VARIABLES:
- PHARMACOKINETIC EVALUATION
The rate and extent of systemic availability of budesonide from the CIR capsule on the seventh day of treatment. The intravenous administration was used as a reference.

- PHARMACODYNAMIC EVALUATION
Systemic effects of budesonide measured as plasma cortisol suppression. The cortisol levels (AUC0-24h) were compared between the baseline day (no treatment) and the last treatment day.
STATISTICAL METHODS

Descriptive.
For budesonide: Standard pharmacokinetic parameters.
For cortisol: The areas under the plasma cortisol concentration curve, 0-24 hours, were calculated.

SUMMARY AND CONCLUSIONS

- PHARMACOKINETIC RESULTS
The systemic exposure of budesonide after oral administration of 9 mg once daily for seven days were on average 41 nmol/L x h (range 13-75 nmol/L x h) in children and 35 nmol/L x h (range 12-63 nmol/L x h) in adults (AUC0-24h). The estimated bioavailability in children was 9% (range 3-17%), and in adults 11% (range 3-21%).

- PHARMACODYNAMIC RESULTS
The mean plasma cortisol (AUC0-24h) decreased from baseline to end of seven days of treatment by 64% (range 37-92%) in children and by 50% (range 18-89%) in adults.

- CONCLUSIONS
The systemic exposure, bioavailability and cortisol suppression after oral administration of 9 mg budesonide CIR did not differ between children and adults with an active Crohn’s disease.

Budesonide given intravenously and as CIR capsule was well tolerated by the patients and no clinically important safety related findings were identified in this study.

DATE OF THE REPORT

2 JAN 2002

(THIS REPORT REPLACE THE 2ND INTERIM REPORT FROM APR 2001)