Synopsis of study report: 204E/96
Location in Module 5:

Study Code:
BY217/FHP002

Report Date:
04-Sep-1996

Title of the study:

Safety and tolerability of the new phosphodiesterase inhibitor (B9302-107) administered to healthy male volunteers as ascending single oral doses

Study center(s):

Inveresk Clinical Research Limited, Edinburgh, UK

Publication (reference):

Not available

Studied period (years):

December 1995 – January 1996

Clinical phase:

I

Objectives:

- Safety and tolerability after single-dose oral administration of ascending dose levels of B9302-107, preliminary data on pharmacokinetics.

Methodology:

Single-blind, placebo-controlled, ascending dose study with randomly interspersed placebo phases.

No. of subjects (total and for each treatment):

4 healthy male subjects

Diagnosis and criteria for inclusion:

Healthy male subjects

Duration of treatment:

Single-dose
The study was terminated after the third period in dose group I, actually. The dose levels 1 mg and 2.5 mg B9302-107 were administered to 4 subjects each, the dose level 5 mg B9302-107 was administered to only 1 subject.

Test product:

Roflumilast

Dose:

Dose levels planned (with randomly interspersed placebo phases):

a) Dose group I (n=4 subjects): 1 mg, 2.5 mg and 5 mg B9302-107
b) Dose group II (n=4 subjects): 10 mg, 15 mg and 20 mg B9302-107

Mode of administration:

p.o.

Batch No.:

066495 (tablet with 0.25 mg)
065495 (tablet with 2.5 mg)

Reference product:

Placebo

Dose:

D0: 4 tablets or 8 tablets

Mode of administration:

p.o.

Batch No.:

067495

Criteria for evaluation:

Safety and tolerability was evaluated by repeated measurements of blood pressure, heart rate, ECG, clinical laboratory investigations and recording of adverse events. The pharmacokinetic

profiles of B9302-107 were determined in 1 subject after dosing of 5 mg and in 2 subjects after dosing of 2.5 mg B9302-107.

Statistical methods:

Descriptive (individual values, medians, 68%-ranges, means, SD, SEM, plots of B9302-107 plasma concentrations).

SUMMARY - CONCLUSIONS

Summary:

Results:

After administration of 1.0 mg B9302-107 one subject complained about diarrhea and one about headache, while two subjects reported no adverse events. Adverse events were more frequent after administration of 2.5 mg B9302-107 and 5.0 mg B9302-107, so that it seemed that the limit of tolerability had been reached with 1.0 mg B9302-107.
As the pharmacokinetic parameters defined in the study protocol could not be calculated due to low sample size, the study provides only preliminary information about the pharmacokinetics of B9302-107.

Conclusions:

B9302-107 when administered as ascending single oral doses to healthy male subjects was well tolerated at a dose level of 1 mg.