Synopsis of study report: BY217/CP-052
Location in Module 5:

Study Protocol No.:
BY217/CP-052

Report Version:
Version 1.0

Title of the study:

Post-study observation of subjects who have reached the primary endpoint under repeated oral doses of 500 µg roflumilast in study BY217/FHP035.

Study center(s):

FARMOVS-PAREXEL, 9300 Bloemfontein, South Africa
SACT, 6529 George, South Africa
Andrology Unit, Department of Urology, 0001 Pretoria, South Africa
Parexel GmbH, 14050 Berlin, Germany
Swiss Pharma Contract, 4123 Allschwil, Switzerland

Publication (reference):

Not applicable

Studied period (years):

16 May 2002 – 3 June 2003

Clinical phase:

Phase I

Objectives:

Long term observation of subjects who have reached the primary endpoint in study BY217/FHP035 for safety reasons.

Methodology:

Standardized semen samples were collected and analyzed according to WHO criteria.

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

A total of 96 subjects (48 had received roflumilast and 48 had received placebo in study BY217/FHP035) was enrolled into the study, of whom 91 completed the study. No treatment (roflumilast or placebo) was administered during this study.

Diagnosis and criteria for inclusion:

Healthy male subjects, aged 18 to 45 years, who took part in study BY217/FHP035 and had reached the primary endpoint [decrease of sperm concentration or progressive motility (grades a + b) by more than 50% of the average of the baseline values at any of the visits during the treatment or follow-up period of study BY217/FHP035] were eligible for inclusion.

Test product:

None

Dose:

Not applicable

Mode of administration:

Not applicable

Batch No.:

Not applicable

Duration of treatment:

Not applicable

Reference product:

Not applicable

Dose:

Not applicable

Mode of administration:

Not applicable

Batch No.:

Not applicable

Criteria for evaluation:

Primary variable

Sperm concentration and progressive motility after a standardized abstinence period of between 72 to 96 hours.

Secondary variables

Semen variables (volume, viscosity, total sperm number, total motility, percentage of alive sperm cells, detection of leucocytes, sperm morphology), male reproductive hormones (testosterone, FSH, LH, Inhibin B), physical examination, body temperature, blood pressure, pulse rate, ECG variables and adverse events.

Statistical methods:

Primary variable

Absolute values and changes from baseline were analyzed descriptively.

Secondary variables

Absolute values and changes from baseline were analyzed descriptively.

SUMMARY - CONCLUSIONS

Summary:

Semen results

No relevant differences were found between the roflumilast- and placebo group for semen variables with respect to mean values, mean differences from baseline values, as well as numbers of clinical relevant cases.

Safety results

A total of 84 adverse events was reported by 45 subjects (50.0 % in the roflumilast group as compared to 43.8 % in the placebo group). A total of 5 subjects discontinued the study, one due to a serious adverse event (placebo group). This adverse event resulted in death (due to a traffic accident), and was not considered to be related to the study. No relevant differences were found between the roflumilast- and placebo group for variables of male reproductive hormones, clinical chemistry, and hematology, as well as ECG, blood pressure and pulse rate.

Conclusions:

A subset of male subjects was observed for 48 weeks primarily with respect to semen variables after being exposed to 500 µg roflumilast or placebo for 12 weeks. No 'early' or 'late' adverse effect of roflumilast on semen- and other safety variables was detected.