Synopsis of study report: 285/ 2004
Location in Module 5:

Study Protocol No.:
BY217/CP-063

Report Version:
1.0

Title of the study:
Palatability of a 125 µg, 250 µg and 500 µg roflumilast suspension in healthy subjects – a double-blind, placebo-controlled, 4-period change-over study

Study center:
Clinical Pharmacology, University of Tübingen, Germany

Publication (reference):
None

Studied period (years):
2004

Clinical phase:
I

Objectives:
Primary
Assessment of a possible gustatory change after the oral application of a suspension, containing 125 µg, 250 µg and 500 µg roflumilast, as compared to placebo, quantitatively measured by a visual analogue scale, assuming a 'neutral' taste before the application of the study medication.

Secondary

Qualitative description of possible gustatory and other sensations after the oral application of a suspension, containing 125 µg, 250 µg, 500 µg roflumilast or placebo, as well as the assessment of safety and tolerability.

Methodology:

Pharmacodynamics:

Visual analogue scale and description

Safety

Medical history, physical examination, blood pressure and pulse rate, adverse events

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

A total of 24 male subjects (with an age range between 19 and 44 years and a weight range between 64 and 115 kg)

Diagnosis and criteria for inclusion:

Healthy male subjects, aged 18-45 years with intact tongue and oral cavity.

Test product:

Roflumilast

Dose:

125µg, 250µg and 500µg

Mode of administration:

Oral

Batch No.:

320200, 120190, 430170

Duration of treatment:

1 day

Reference product:

Placebo

Dose:

Not applicable

Mode of administration:

Oral

Batch No.:

130290

Criteria for evaluation:

Primary variable

Distance (in millimeters) between 0 and the mark, applied by the subject on an unscaled VAS of 10 cm. The subject was to be asked to give a visual representation of his perceived change of gustatory sensation at 2, 5, 15, 30, 60, 120 and 240 minutes after the oral application of a suspension, containing 125 µg, 250 µg, 500 µg roflumilast, or placebo, assuming a 'neutral' taste before the application of the study medication.

Secondary variables

- Qualitative description of possible gustatory and other sensations at 2, 5, 15, 30, 60, 120 and 240 minutes after the oral application of a suspension, containing 125 µg, 250 µg, 500 µg roflumilast or placebo
- Measurements of systolic and diastolic blood pressure, and pulse rate
- Adverse events

Statistical methods:

Descriptive statistics

SUMMARY - CONCLUSIONS

Summary:

Pharmacodynamics

With respect to the determination of changes from baseline in gustatory sensation (quantitative evaluation), some subjects could distinguish between placebo and roflumilast, with a most pronounced change at 5 minutes after the administration of roflumilast. However, no dose-dependent trend was discernable, and a big spread of absolute values in all groups (placebo and roflumilast) was seen. With respect to the description of gustatory sensations (qualitative evaluation), some subjects could distinguish between placebo and roflumilast at 5 and 15 minutes after the administration of study medication. The gustatory sensation of

roflumilast at these time points was described as ‘prickly’, ‘furred’, ‘numb’, ‘hot (spicy)’ or ‘bitter’.

Safety

No serious adverse events occurred during the course of the study. A total of 6 subjects reported a total of 7 adverse events. No noteworthy differences were found between the 125 µg - and 250 µg roflumilast- and placebo groups. No adverse events were observed in the 500 µg roflumilast group. Overall, ‘headache’ was the most frequently reported adverse event throughout the study, with 2 subjects of the placebo group reporting 2 events, as compared to 1 subject each in the 125 µg and 250 µg roflumilast group. No differences were observed between placebo and roflumilast with respect to systolic and diastolic blood pressure and pulse rate.

Conclusions:

Some subjects could taste roflumilast at about 5 to 15 minutes after the oral intake of a roflumilast suspension. No dose-dependent trend was discernable. A large inter-individual variability was observed. The gustatory sensation of roflumilast at these time points was described as ‘prickly’, ‘furred’, ‘numb’, ‘hot (spicy)’ or ‘bitter’. Roflumilast was safe and well tolerated.