This Summary of Clinical Study Report is provided for patients and healthcare professionals to demonstrate the transparency efforts of the Menarini Group. This document is not intended to replace the advice of a healthcare professional and can't be considered as a recommendation. Patients must always seek medical advice before making any decisions on their treatment. Healthcare Professionals should always refer to the specific labelling information approved for the patient's country or region. Data in this document can not be considered as prescribing advice.

The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

1 Study Synopsis

Clinical Trial Number: BCBe/03/Pan-CPI/003

Sponsor's Responsible Persons: [redacted]

Test Drug: Helopanflat® mono 10.000 (Nordmark).

Dose Test Drug: 4 enteric-coated tablets with porcine pancreatin with a total activity of 40.000 Ph.Eur. units lipase, at least 36.000 Ph.Eur. units amylase, at least 2.000 Ph.Eur. units protease.

Dose Comparator Drug: 4 enteric-coated placebo tablets.

Active ingredient: pancreatin
Mode of administration: oral

Dose: 4 tablets for 1 single administration

Batch no.: **280104**

Comparator Drug: matching Placebo

Dose: 4 gastro-resistant film-coated placebo tablets.

Batch no.:101203

Indication Studied: Pancreatic exocrine insufficiency due to chronic pancreatitis

Clinical Trial Phase: Phase IV

Number of Patients: Planned: 20 evaluable patients
Analyzed: 7 patients after study discontinuation

(study was discontinued because in a parallel performed similar study the used screening elastase testing showed false positive results, hence the efficacy of the test product was not significant)

Enrolment of First Patient: 01.02.2005

Last Visit of Last Patient: 21.07.2005

Date of Early Termination The study was prematurely discontinued on 31.10.05

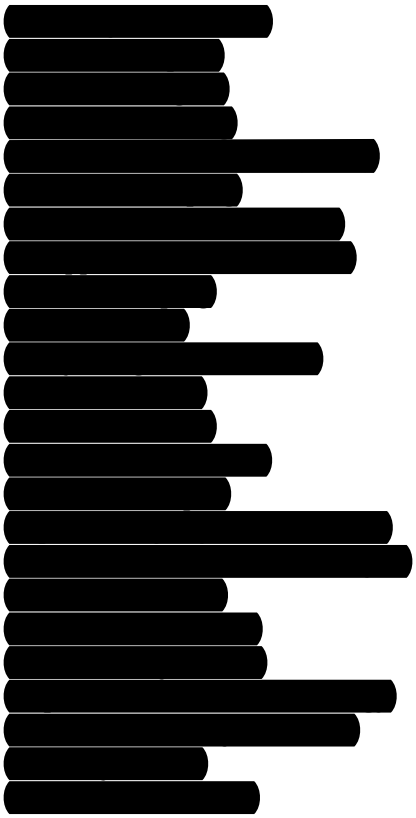
Duration of Treatment for Each Patient: 2 single applications separated by a wash-out phase of three days (cross-over design vs. placebo)

9-19 days

Number of Clinical Trial Centers: 3 centres in Ger and ~~CZ~~ PL

Coordinating Investigator:

Investigators:



Objectives / Criteria for evaluation (efficacy and safety)

Primary objective:

- To evaluate the difference between ^{13}C-exhalation (in terms of cumulative percentage of ^{13}C-dose exhaled per hour after 6 hours starting with the end of the test meal) as a marker of lipid digestion and absorption during treatment with verum and placebo.

Secondary objective(s):

- Difference between the maximum percentage of ^{13}C-dose exhaled per hour within 8 hours during treatment with verum and placebo.
- Difference between ^{13}C-exhalation (in terms of cumulative percentage of ^{13}C-dose exhaled per hour in 1h-intervals, for 8 hours) during treatment with verum and placebo.
- Safety and tolerability of trial medication versus placebo (vital signs, laboratory parameters, physical examinations, ECG, Adverse Events).

Methodology

- Standardised ^{13}C-mixed triglyceride breath test performed twice with patients with known and documented pancreatic exocrine insufficiency, once with verum, once with placebo in a randomised double blind cross-over design.
- Collection of breath samples before and every 30 min for 8 hours after ingestion of a test meal with ^{13}C-mixed triglycerides, additional standardised meal allowed after 6.5 h.
- Trial medication should be taken unchewed in the middle of the test meal at 08:00 +/- 2 hrs.
- Measurement of ^{13}C-concentration in all breath samples by isotope-selective non-dispersive infrared spectrometry.
- Documentation of Adverse Events by the investigator.

Diagnosis and main inclusion criteria

1. Chronic pancreatitis documented by a score of 4 or more added-up using the following scoring system (modified according to Layer et al. (1994)):
2. Faecal elastase 1 test result < 100 µg/g faeces at Screening.

Statistical methode

The primary objective of the double blind, randomised cross-over trial is to confirm the superiority of the trial drug versus placebo with regard to the difference in 13C-exhalation (in terms of cumulative percentage of 13C-dose exhaled per hour after 6 hours starting with the end of the test meal). The difference in 13C-exhalation will be assessed by an Analysis of Covariance (or similar non-parametric approaches).

summary conclusions

Efficacy results

Due to the prematurely discontinuation of the study only 7 patients instead of 20 patients were enrolled.
Superiority of Helopanflat®mono vs. placebo could not be shown for the primary efficacy parameter. All data were listed but the planned statistical tests were not performed.
At vistit 4 after 6 h the CO2 in the placebo group was 3,13% and in the Pancreatin group 3,45 and at Visit 5 for the placebo group 3,35 and for the pancreatin group 2,93.

Safety results

No SAE occurred during the course of the trial. No remarkable changes in vital signs, ECG or physical findings occurred during the trial. The evaluation of routine laboratory examination, physical examinations, ECG recordings and measurement of vital signs (blood pressure, pulse rate and body weight) revealed that administration of gastro-resistant film-coated tablet with porcine pancreatin (Helopanflat®mono) was well tolerated and safe.