# Summary of Clinical Study Results (Version 1.0)

## Study Protocol BY1023/DE004

## Clinical Study Report 492/2007

**Title of the study:** Symptom reduction in hospitalized patients suffering from symptomatic non-erosive or erosive gastroesophageal reflux disease treated with pantoprazole 20 or 40 mg od for 7 days.

## EudraCT Number: 2005-004856-11

## Clinicaltrials.gov Identifier: NCT00326027

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**Title of the study:** Symptom reduction in hospitalized patients suffering from symptomatic non-erosive or erosive gastroesophageal reflux disease treated with pantoprazole 20 or 40 mg od for 7 days.

**Investigator and study centers:**

The study was a multi-center study in 35 participating centers in Germany. Only 9 centers thereof were active and recruited patients.

**Coordinating investigator(s):**

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**Publication (reference):** Not applicable.

**Studied period:** 10-OCT-2006 to 02-JUL-2007

**Clinical phase:** III

**Objectives:**

This was the first study to prove fast symptom reduction in hospitalized patients suffering from NERD (non-erosive gastroesophageal reflux disease) or GERD (gastroesophageal reflux disease) after 1 day of treatment with pantoprazole 20 mg (NERD) or with pantoprazole 40 mg (GERD A-D).

**Methodology:**

Open, multi-center, stratified (GERD/NERD).

NERD: 7 days treatment with pantoprazole 20 mg

GERD A-D: 7 days treatment with pantoprazole 40 mg

**No. of patients planned and analyzed:**

A number of 350 patients (at least 18 years of age) in 35 study centers were planned to be included into the ITT (intention-to-treat) population to obtain 285 patients PP (per-protocol).

Due to very slow recruitment only 29 patients in 9 study centers could be included in the study. Therefore, the study was terminated because it became obvious that the target number of patients would not be reached in a reasonable time. One patient did not take any medication, thus 28 patients were in the safety set.

**Analyzed set**

| | Total set | Safety set |
|---|---|---|
| Group NERD (pantoprazole 20 mg) | 7 | 7 |
| Group GERD (pantoprazole 40 mg) | 21 | 21 |
| Missing | 1 | - |
| Total | 29 | 28 |

**Diagnosis and main criteria for inclusion:**

- written informed consent by the patient for study participation, prior to protocol specific procedures;
- inpatients of at least 18 years of age (hospitalization during the entire study period of 7 days is mandatory);
- symptomatic (heartburn, acid regurgitation or dysphagia for at least 1 day since admission to the hospital) NERD or GERD (LA [Los Angeles] grade A-D).

**Test product, dose, mode of administration, batch no.:**

Pantoprazole 20 mg, once daily, oral, 00300101

Pantoprazole 40 mg, once daily, oral, 00300102

**Reference product, dose, mode of administration, batch no.:**

Not applicable.

**Duration of treatment:**

7 days of treatment with either pantoprazole 20 mg (NERD patients) or pantoprazole 40 mg (GERD patients)

**Criteria for evaluation:**

Primary variable

- symptom reduction from reflux disease related symptoms measured as assessed by ReQuest™-GI after 1 day of treatment.

For the primary variable a separate analysis was done for the subgroups NERD and GERD.

Secondary variables

- symptom reduction from reflux disease related symptoms as assessed by ReQuest™-GI after 2, 3, 4, 5, 6 and 7 days of treatment were analyzed analogous to the primary variable;
- the symptom relief rates as assessed by ReQuest™ after 7 days of treatment and the respective 95% confidence intervals were calculated;
- the relief rates from reflux disease related complaints after 7 days of treatment (as assessed by the investigator) and the respective 95% confidence intervals were calculated.

Five further secondary variables could not be analyzed as planned due to the low number of patients.

**Statistical methods:**

Due to the low number of patients all analyses were based on the safety set.

Only descriptive analyses have been performed for all efficacy and safety variables.

## SUMMARY – CONCLUSIONS

Demography and baseline characteristics

**Demographic and other baseline characteristics by gender (safety set, N = 28)**

| Demographic variable | Overall N = 28 | Male N = 15 | Female N = 13 |
|---|---|---|---|
| Age [years], mean (SD) | 66.79 (14.11) | 57.61 (11.63) | 77.39 (7.94) |
| Height [cm], mean (SD) | 169.68 (10.74 | 177.20 (8.65) | 161.00 (4.47) |
| Weight [kg], mean (SD) | 75.46 (13.15) | 80.20 (12.63) | 70.00 (11.94) |
| BMI [kg/m²], mean (SD) | 26.22 (3.90) | 25.58 (3.72) | 26.96 (4.11) |

N: number of patients, SD: standard deviation

### Study results

Efficacy results

A symptom reduction was observed after one day of treatment as assessed by all three ReQuest™ scores (ReQuest™-GI, ReQuest™-WSO, ReQuest™ total score) in both treatment groups. With regard to the primary variable, ReQuest™-GI, the pre-post difference was numerically higher in the NERD group treated with pantoprazole 20 mg (-2.20) than in the GERD group treated with pantoprazole 40 mg (-0.99). Also with regard to the course of symptoms during the 7 days of treatment (secondary variables), there was a reduction of symptoms over time. Due to the very low number of patients and thus the exploratory character of the analyses, it is not possible to draw any clinical relevant conclusion concerning the primary and secondary variables.

Safety results

No death or SAEs were observed during the course of the study. 5 treatment-emergent AEs were experienced by 5 out of 28 patients (17.9%) included in the safety set. In the $P_{20}$ group, 1 patient experienced 1 AE and in the $P_{40}$ group, 4 patients experienced 4 AEs.

**Treatment-emergent AEs (safety set N = 28)**

| | $P_{20}$ group (N = 7) | | $P_{40}$ group (N = 21) | |
|---|---|---|---|---|
| | **Obs** | **%** | **Obs** | **%** |
| AEs | 1 | 14.3 | 4 | 19.0 |
| SAEs | - | - | - | - |
| Deaths | - | - | - | - |
| AEs with causality[a] suggested by the investigator | - | - | - | - |
| AEs leading to discontinuation | - | - | 1 | 4.8 |

[a] AEs assessed by the investigator as “likely” ore “definitely” related to the study medication.

AE = adverse event, N = number of patients, Obs = number of patients with events, $P_{20}$ group = patients in stratum NERD (pantoprazole 20 mg), $P_{40}$ group = patients in stratum GERD (pantoprazole 40 mg), SAE = serious adverse event

As assessed by the investigator, 3 (60%) of the treatment-emergent AEs showed ‘unrelated’ relation to the study medication (all in the $P_{40}$ group: GGT increased, Cholecystolithiasis, Gastroenteritis). 2 AEs (40%) were assessed as ‘unlikely’ related to the study medication (1 AE in $P_{20}$ group: Meteorism; 1 AE in $P_{40}$ group: Allergic reaction). No ‘likely’ or ‘definite’ relation to the study medication was documented.

The intensity of AE symptoms as reported by the investigator was ‘mild’ for 1 case (1 patient of the $P_{20}$ group ), ‘moderate’ for 3 cases (3 patients of the $P_{40}$ group ) and ‘severe’ for 1 case (1 patient of the $P_{40}$ group ).

1 patient (3.6% of the safety set) of the $P_{40}$ group prematurely discontinued the study due to the treatment emergent AE allergic reaction.

According to the investigators, none of the respective AE symptoms was assessed as ‘definitely’ related to the study medication.

No vital sign parameter assessed showed systematically or relevant changes during the course of the study.

In conclusion, both doses of pantoprazole were well tolerated and safe.

**Conclusions:**

Due to the low number of patients only descriptive analyses of efficacy and safety could be applied. However, numerical trends were observed indicating a fast symptom reduction in hospitalized patients suffering from GERD and NERD and treated with pantoprazole over 7 days. Pantoprazole 20 mg and pantoprazole 40 mg were well tolerated and safe during a reatment duration of 7 days. The present study did not reveal any suspicion of hitherto unknown risks for the intake of pantoprazole.