



Clinical trial results:

The effect of Prucalopride (Resolor) on gastric motor function and gastric sensitivity

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-002705-65 |
| Trial protocol | BE |
| Global end of trial date | 27 July 2015 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 11 February 2021 |
| First version publication date | 11 February 2021 |

Trial information

Trial identification

| | |
|-----------------------|---------------------|
| Sponsor protocol code | PrucaloprideGastro1 |
|-----------------------|---------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04429802 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UZLeuven KULeuven |
| Sponsor organisation address | Herestraat 49, Leuven, Belgium, 3000 |
| Public contact | Jan Tack, TARGID, 0034 16344225, jan.tack@kuleuven.be |
| Scientific contact | Florencia Carbone, TARGID, 0034 16330824, florencia.carbone@kuleuven.be |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 03 February 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 July 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate the effect prucalopride on the gastric motor function. The gastric manometry and the gastric barostat will be used in order to gain more information about its effect on gastric accommodation and gastric sensitivity.

Protection of trial subjects:

not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 18 October 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Belgium: 17 |
| Worldwide total number of subjects | 17 |
| EEA total number of subjects | 17 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 17 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Healthy volunteers (HVs), recruited by public advertisement

Pre-assignment

Screening details:

HVs had to be devoid of GI symptoms and of the use of medications known to influence the GI motility.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | gastric barostat study |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | No |
| Arm title | prucalopride 2 mg |

Arm description:

single-blind randomized controlled cross-over gastric barostat study (placebo vs. prucalopride 2 mg).

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | prucalopride 2 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

prucalopride 2 mg, taken orally only once at timepoint 2 hours before the meal during the barostat measurement.

| | |
|------------------|---------|
| Arm title | placebo |
|------------------|---------|

Arm description:

single-blind randomized controlled cross-over gastric barostat study (placebo vs. prucalopride 2 mg).

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

placebo tablet, taken orally only once at timepoint 2 hours before the meal during the barostat measurement.

| Number of subjects in period 1 | prucalopride 2 mg | placebo |
|--------------------------------|-------------------|---------|
| Started | 12 | 12 |
| Completed | 12 | 12 |

Period 2

| | |
|------------------------------|------------------------------------|
| Period 2 title | intra gastric pressure measurement |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | No |
| Arm title | prucalopride 2 mg |

Arm description:

single-blind randomized controlled cross-over intra gastric pressure measurement study (placebo vs. prucalopride 2 mg).

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | prucalopride 2 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

prucalopride 2 mg, taken orally only once at timepoint 2 hours before the meal during the IGP measurement.

| | |
|------------------|---------|
| Arm title | placebo |
|------------------|---------|

Arm description:

single-blind randomized controlled cross-over intra gastric pressure measurement study (placebo vs. prucalopride 2 mg).

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

placebo tablet, taken orally only once at timepoint 2 hours before the meal during the IGP measurement.

| Number of subjects in period 2 | prucalopride 2 mg | placebo |
|---------------------------------------|-------------------|---------|
| Started | 15 | 15 |
| Completed | 15 | 15 |

Baseline characteristics

Reporting groups^[1]

| | |
|-----------------------|------------------------|
| Reporting group title | gastric barostat study |
|-----------------------|------------------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: In total 17 different subjects participated in the whole study.

10 subjects participated in both part 1 and part 2.

In total 12 subjects participated in part 1, i.e. the barostat study part

In total 15 subjects participated in part 2, i.e. the intragastric measurement part

| Reporting group values | gastric barostat study | Total | |
|--|------------------------|-------|--|
| Number of subjects | 12 | 12 | |
| Age categorical | | | |
| healthy volunteers | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 12 | 12 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| healthy volunteers | | | |
| Units: years | | | |
| arithmetic mean | 32 | | |
| standard deviation | ± 1.7 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 5 | 5 | |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | prucalopride 2 mg |
| Reporting group description: single-blind randomized controlled cross-over gastric barostat study (placebo vs. prucalopride 2 mg). | |
| Reporting group title | placebo |
| Reporting group description: single-blind randomized controlled cross-over gastric barostat study (placebo vs. prucalopride 2 mg). | |
| Reporting group title | prucalopride 2 mg |
| Reporting group description: single-blind randomized controlled cross-over intragastric pressure measurement study (placebo vs. prucalopride 2 mg). | |
| Reporting group title | placebo |
| Reporting group description: single-blind randomized controlled cross-over intragastric pressure measurement study (placebo vs. prucalopride 2 mg). | |

Primary: difference in gastric pressure and compliance between prucalopride vs placebo

| | |
|---|---|
| End point title | difference in gastric pressure and compliance between prucalopride vs placebo |
| End point description: In the gastric sensitivity studies, for each 2 min distending period, the mean intragastric volume was calculated. The perception threshold was defined as the first level of pressure and the corresponding volume that evoked a perception score of 1 or more. Discomfort threshold was defined as the first level of pressure and the corresponding volume that provoked a sensation score of five or more. The gastric compliance of the subjects was calculated as the slope of the volume/pressure curve. The gastric sensitivity to distention of the subjects was calculated as the slope of the sensitivity scores/pressure curve. | |
| End point type | Primary |
| End point timeframe: Cross over study. Results of the gastric pressures during part 1, i.e. barostat study between placebo and prucalopride | |

| End point values | prucalopride 2 mg | placebo | | |
|--------------------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 12 | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 9.8 (± 0.4) | 10 (± 0.5) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | gastric pressures. cross over. pruc vs placebo |
| Comparison groups | prucalopride 2 mg v placebo |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 24 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.61 ^[1] |
| Method | t-test, 2-sided |

Notes:

[1] - In all analyses, $p < 0.05$ was considered significant.

all analyses resulted in not significant differences between prucalopride and placebo

Primary: effect of prucalopride on distal stomach intragastric pressure

| | |
|-----------------|--|
| End point title | effect of prucalopride on distal stomach intragastric pressure |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

During the second hour before the meal. This is one hour after prucalopride (2 mg)/placebo intake

| End point values | prucalopride 2 mg | placebo | | |
|---------------------------------------|---------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 ^[2] | 15 ^[3] | | |
| Units: area under the IGP curve (AUC) | | | | |
| arithmetic mean (standard deviation) | 345.6 (\pm 57.2) | 126.7 (\pm 80) | | |

Notes:

[2] - cross over study

[3] - cross over study

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Effect of prucalopride on distal stomach IGP |
|----------------------------|--|

Statistical analysis description:

During the second hour before the meal, the AUC was increased after prucalopride treatment compared to placebo (n=15, AUC prucalopride: 345.6 \pm 57.2 mmHg.min⁻¹ and AUC placebo: 126.7 \pm 80 mmHg.min⁻¹; $p=0.05$).

| | |
|---|-----------------------------|
| Comparison groups | prucalopride 2 mg v placebo |
| Number of subjects included in analysis | 30 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.05 |
| Method | t-test, 2-sided |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For each individual, corresponds to timeframe of study participation (from signing of informed consent until last visit).

Adverse event reporting additional description:

Symptoms scored during measurements using VAS are not considered adverse events.

After prucalopride intake, some healthy volunteers suffered from nausea and vomiting resulting in a premature stop of the barostat measurement. These symptoms are considered as adverse events.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 23 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | subjects participating in barostat study |
|-----------------------|--|

Reporting group description:

Adverse events after the intake of prucalopride was only seen during the barostat study.

Suggesting that the gastric volume measurements after the meal during treatment with prucalopride may reflect nausea-related events, induced by prucalopride in the presence of a distending barostat bag in the stomach, rather than a true effect of prucalopride on the proximal stomach of the subjects. This interpretation is supported by our observations in the IGP studies.

| Serious adverse events | subjects participating in barostat study | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | subjects participating in barostat study | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 12 (58.33%) | | |
| Gastrointestinal disorders | | | |
| nausea | | | |
| subjects affected / exposed | 7 / 12 (58.33%) | | |
| occurrences (all) | 7 | | |
| Vomiting | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 4 / 12 (33.33%) | | |
| occurrences (all) | 4 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported