



Clinical trial results:

Improving the tolerability of the oral targeted anti-cancer drug pazopanib by food intake (DIET)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-004108-20 |
| Trial protocol | NL |
| Global end of trial date | 09 August 2018 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 26 January 2020 |
| First version publication date | 26 January 2020 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | UMCN-AKF13.05 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02138526 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Radboudumc |
| Sponsor organisation address | Geert Grooteplein Zuid 10, Nijmegen, Netherlands, |
| Public contact | Angela Colbers, Radboud University Nijmegen Medical Centre, +31 243616405, angela.colbers@radboudumc.nl |
| Scientific contact | Angela Colbers, Radboud University Nijmegen Medical Centre, +31 243616405, angela.colbers@radboudumc.nl |

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 | 15 November 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 09 August 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 August 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Part A: To determine the equivalent dose of pazopanib when taken with a continental breakfast compared to 800 mg in fasted state.

Part B: To evaluate whether food can reduce the side effects diarrhea and nausea.

Protection of trial subjects:

Part A

Participating patients will be asked for a hospital admission for two days to collect the blood samples. All blood samples will be drawn from a once placed intravenous cannula. A total of 10 blood samples will be taken per admission day. The burden for the participants of this part of the study is considered to be mild. In general the risk for participation in this study is regarded moderate.

The risk of suboptimal dosing is minimized by the run in of three patients at 600 mg OD with food. Benefits associated with participating in this study are that patients and their treating physician get insight into pazopanib exposure when taken with a continental breakfast.

Part B

The participating patients are asked to keep a record on their defecation pattern and nausea experiences during both treatment regimens, at the end of the study period their preference is asked. Therefore the burden for the participants of this part of the study is considered to be low.

In general the risk for participation in this study is regarded negligible.

Patients receive a bioequivalent dose pazopanib also normal C_{tr} though levels will be monitored.

Benefits associated with participating in this study are that patients might experience less side effects and the intake of pazopanib will be more easily incorporated in their normal life style.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 01 January 2014 |
| 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 | Netherlands: 97 |
| Worldwide total number of subjects | 97 |
| EEA total number of subjects | 97 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|----|
| wk | |
| 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) | 68 |
| From 65 to 84 years | 28 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in two parts. First, a PK study was performed to establish the bioequivalent dose of pazopanib when ingested with a CB (part 1). This part was designed as an open-label, crossover, multicenter, phase I study conducted in two centers in the Netherlands (Radboudumc (Nijmegen) and Leiden University Medical Center (Leiden)).

Pre-assignment

Screening details:

Adult patients (≥ 18 years) receiving 800 mg pazopanib o.d. with an ECOG performance status of 0–2. The use of proton pump inhibitors was allowed when the proton pump inhibitor was used at the same time throughout the study. Use of substances known to alter Cytochrome P 3A4 metabolism were prohibited. Patients with GI abnormalities were excluded.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | screening |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

nap

Arms

| | |
|-----------|----------|
| Arm title | baseline |
|-----------|----------|

Arm description:

baseline

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | pazopanib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

800mg once daily oral without food

| Number of subjects in period 1 | baseline |
|--------------------------------|----------|
| Started | 97 |
| Completed | 78 |
| Not completed | 19 |
| Lost to follow-up | 1 |
| Lack of efficacy | 18 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | PKcurves |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-------------------------|
| Are arms mutually exclusive? | No |
| Arm title | pazopanib 800mg fasting |

Arm description:

pazopanib 800mg fasting

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | pazopanib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

800mg once daily oral without food

| | |
|------------------|------------------------|
| Arm title | pazopanib 600mg + food |
|------------------|------------------------|

Arm description:

pazopanib 600mg + food

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

Dosage and administration details:

600mg once daily oral with food

| Number of subjects in period 2 | pazopanib 800mg fasting | pazopanib 600mg + food |
|---------------------------------------|-------------------------|------------------------|
| Started | 78 | 78 |
| Completed | 78 | 78 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | screening |
|-----------------------|-----------|

Reporting group description: -

| Reporting group values | screening | Total | |
|---|-----------|-------|--|
| Number of subjects | 97 | 97 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 60 | | |
| full range (min-max) | 28 to 85 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 30 | 30 | |
| Male | 67 | 67 | |

End points

End points reporting groups

| | |
|------------------------------|-------------------------|
| Reporting group title | baseline |
| Reporting group description: | baseline |
| Reporting group title | pazopanib 800mg fasting |
| Reporting group description: | pazopanib 800mg fasting |
| Reporting group title | pazopanib 600mg + food |
| Reporting group description: | pazopanib 600mg + food |

Primary: AUC

| | |
|------------------------|---------|
| End point title | AUC |
| End point description: | |
| End point type | Primary |
| End point timeframe: | 24h |

| End point values | pazopanib 800mg fasting | pazopanib 600mg + food | | |
|---|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 78 | 78 | | |
| Units: mg*h/L | | | | |
| geometric mean (geometric coefficient of variation) | 821 (± 36) | 895 (± 38) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | GMR |
| Comparison groups | pazopanib 800mg fasting v pazopanib 600mg + food |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[1] |
| P-value | < 0.1 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | Median difference (final values) |
| Point estimate | 1.09 |

| Confidence interval | |
|---------------------|---------|
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.02 |
| upper limit | 1.17 |

Notes:

[1] - intrasubject comparison, not 156 different subjects in analysis

[2] - nap

Adverse events

Adverse events information

Timeframe for reporting adverse events:

entire study

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

Dictionary used

| | |
|-----------------|------|
| Dictionary name | none |
|-----------------|------|

| | |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | all patients |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | all patients | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 79 (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 | all patients | | |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 79 (7.59%) | | |
| Cardiac disorders | | | |
| hypertension | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | |
| occurrences (all) | 3 | | |
| General disorders and administration site conditions | | | |
| fatigue | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences (all) | 1 | | |
| hair discoloration | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| pneumonia | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 21 June 2018 | <ol style="list-style-type: none">1. Change in in- and exclusion criteria When according to the treating physician a patient is eligible for pazopanib treatment, the patient is eligible for study participation.2. Added secondary objective Progression free survival was added as an secondary objective. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported