



Clinical trial results:

A randomized, multicenter, open-label, phase II study of the optimal scheme of administration of pazopanib in thyroid carcinoma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-003162-41 |
| Trial protocol | FR |
| Global end of trial date | 10 July 2019 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 25 March 2021 |
| First version publication date | 25 March 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | ET12-058 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01813136 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Centre Léon Bérard |
| Sponsor organisation address | 28 rue Laennec, LYON, France, 69008 |
| Public contact | Dr C. de la FOUCHARDIERE, Centre Léon Bérard, +33 4 78 78 28 28, DRCIreglementaire@lyon.unicancer.fr |
| Scientific contact | Dr C. de la FOUCHARDIERE, Centre Léon Bérard, +33 4 78 28 28, DRCIreglementaire@lyon.unicancer.fr |

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 | 24 June 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 July 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 July 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the time to treatment failure in patients with continuous pazopanib versus intermittent pazopanib treatment

Protection of trial subjects:

Information of patient and informed consent signature will be performed prior to any study-specific procedure. The patient will be orally provided by the investigator with the appropriate information; in addition, he will be given written information and an informed consent form. After a sufficient time to think, the patient will give his written consent, by dating and signing the informed consent form. This form will also be signed and dated by the investigator, preferentially on the same day, and a copy will be given to the patient (the original form will be archived in the patient medical file).

All screening examinations will be performed within 15 days prior to first pazopanib administration (day 1). With these exams, the investigational staff will be able to confirm the patient's eligibility, to assess the extent of disease and determine the baseline signs and symptoms.

If all the selection criteria are fulfilled, the investigator will proceed to the inclusion registration.

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | France: 168 |
| Worldwide total number of subjects | 168 |
| EEA total number of subjects | 168 |

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) | 167 |
| From 65 to 84 years | 0 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All screening examinations will be performed within 15 days prior to first pazopanib administration (day 1). With these exams, the investigational staff will be able to confirm the patient's eligibility, to assess the extent of disease and determine the baseline signs and symptoms. If all the selection criteria are fulfilled, the investigator will

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Treatment |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-----------|
| Arm title | Pazopanib |
|-----------|-----------|

Arm description:

First, all patients included in the study will be treated with pazopanib at the dose of 800 mg daily for 6 cycles.

| | |
|--|------------------------------------|
| Arm type | Pazopanib for all included patient |
| Investigational medicinal product name | PAZOPANIB |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Buccal use |

Dosage and administration details:

All patients included in the study will be treated with pazopanib at the dose of 800 mg daily for 6 cycles.

| Number of subjects in period 1 | Pazopanib |
|--------------------------------|-----------|
| Started | 168 |
| Completed | 100 |
| Not completed | 68 |
| Early toxicity | 20 |
| Early progressive disease | 34 |
| Death | 3 |
| Other reasons | 11 |

Period 2

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

Arms

| | |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A = Reference strategy |

Arm description:

Continuation of oral administration of pazopanib at the dose of 800 mg daily, until disease progression or unacceptable toxicity.

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

Dosage and administration details:

Continuation of oral administration of pazopanib at the dose of 800 mg daily, until disease progression or unacceptable toxicity.

| | |
|------------------|-------------------------------|
| Arm title | Arm B = Experimental strategy |
|------------------|-------------------------------|

Arm description:

Temporary discontinuation of pazopanib until a first off-treatment progression. As soon as this progression occurs, daily oral administration of 800 mg pazopanib will be reintroduced for six additional cycles. If an on-treatment progression occurs before the end of the 6th cycle, pazopanib will be permanently discontinued. However, in case of long term stability or response, patient will remain in the study and will be treated with intermittent 6-cycle periods until on-treatment progression or unacceptable toxicity.

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

Dosage and administration details:

Temporary discontinuation of pazopanib until a first off-treatment progression. As soon as this progression occurs, daily oral administration of 800 mg pazopanib will be reintroduced for six additional cycles. If an on-treatment progression occurs before the end of the 6th cycle, pazopanib will be permanently discontinued. However, in case of long term stability or response, patient will remain in the study and will be treated with intermittent 6-cycle periods until on-treatment progression or unacceptable toxicity.

| Number of subjects in period 2 | Arm A = Reference strategy | Arm B = Experimental strategy |
|--------------------------------|----------------------------|-------------------------------|
| | | |
| Started | 50 | 50 |
| Completed | 50 | 50 |

Baseline characteristics

End points

End points reporting groups

| | |
|---|-------------------------------|
| Reporting group title | Pazopanib |
| Reporting group description: First, all patients included in the study will be treated with pazopanib at the dose of 800 mg daily for 6 cycles. | |
| Reporting group title | Arm A = Reference strategy |
| Reporting group description: Continuation of oral administration of pazopanib at the dose of 800 mg daily, until disease progression or unacceptable toxicity. | |
| Reporting group title | Arm B = Experimental strategy |
| Reporting group description: Temporary discontinuation of pazopanib until a first off-treatment progression. As soon as this progression occurs, daily oral administration of 800 mg pazopanib will be reintroduced for six additional cycles. If an on-treatment progression occurs before the end of the 6th cycle, pazopanib will be permanently discontinued. However, in case of long term stability or response, patient will remain in the study and will be treated with intermittent 6-cycle periods until on-treatment progression or unacceptable toxicity. | |

Primary: Primary end point

| | |
|--|----------------------------------|
| End point title | Primary end point ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: Time to permanent treatment discontinuation due to any cause after randomization in each arm | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Efficacy analysis (including response rate) will be conducted using the intention-to-treat principle (ITT). All patients will be taken in the calculation. Safety analysis will be performed on all included patients who received at least one dose of study treatment. Primary endpoint will be evaluated using Kaplan-Meier method. Time to treatment failure curves will be compared between arms using a log-rank test. Median survival will be presented in each arm with its 95% Confidence Interval.

| End point values | Arm A = Reference strategy | Arm B = Experimental strategy | | |
|----------------------------------|----------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 50 | | |
| Units: Time to Treatment Failure | 50 | 50 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

The investigator collects (spontaneous patient report or questioning) and immediately notifies the sponsor of all SAEs, in a written report, whether or not they are deemed to be attributable to research and which occur during the study.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Prior to randomization, 163 patients had at least one treatment-related adverse event, 121 patients had at least one grade ≥ 3 AE and 91 patients had at least one related grade ≥ 3 AE. After randomization, 96.0% of patients presented at least one related AE. Grade ≥ 3 AEs were reported for 61% of patients. 36.0% of patients presented at least one related AE of grade ≥ 3 . SAE were reported for 43.0% of patients and related SAEs for 21.0% of patients.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 09 August 2013 | Modify 2 inclusion criteria Add a liver test during cycle 2 (D15) following the publication of the new BI (v10 of 02/22/2013) |
| 17 February 2014 | Modification of the inclusion criterion I2: confirmation of the diagnosis by a regional referent made non-compulsory PET performance becomes optional on inclusion and before randomization Participation in the ancillary study made optional |
| 24 July 2015 | Remove inclusion criterion I3 Annual update of the pazopanib investigator brochure (v12 of 12/17/2014) having an impact on patient safety Extend the recruitment period by 24 months and consequently the duration of the study (without modification of the follow-up) |
| 12 August 2016 | Annual update of the pazopanib investigator brochure having an impact on patient safety |
| 08 November 2017 | Update of the pazopanib investigator brochure (Votrient Ed 15 of 10/11/2016) having an impact on the reference information on safety and the protocol (without impact on the benefit / risk balance) Update of the vigilance rules following Decree 2016-1537 of November 16, 2016 relating to research involving humans Extension of the inclusion period by 18 months and consequently of the duration of the study (without modification of the follow-up) |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported