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 inform 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 questionning) and immediately notifies the sponsor of all SAEs, in a written report, wether or not theay are deemed to be attributable to research and wich occur during the study.

Assessment type	Systematic

Dictionary used

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