Clinical trial results:
PHASE II STUDY EVALUATION OF EFFICACITY AND TOLERANCE OF REGORAFENIB FOR 70 YEARS OLD AND MORE PATIENTS WITH A METASTATIC COLORECTAL ADENOCARCIMA

Summary

EudraCT number	2015-002086-29
Trial protocol	FR
Global end of trial date	17 October 2018

Results information

Result version number	v1 (current)
This version publication date	02 April 2022
First version publication date	02 April 2022

Trial information

Trial identification

Sponsor protocol code	FFCD1404

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02788006
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fédération Francophone de Cancérologie Digestive (FFCD)
Sponsor organisation address	7 Bd Jeanne d'Arc, Dijon, France, 21000
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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	21 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2017
Global end of trial reached?	Yes
Global end of trial date	17 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This multicenter single-arm phase II enrolled patients ≥70 years old after the failure of fluoropyrimidine-based chemotherapy, anti-VEGF, and anti-EGFR treatment. The primary endpoint was disease control rate (DCR) 2 months after initiation of regorafenib (160 mg/day, 3 weeks on/1 week off).

The mai objective is to assess the efficacy and safety of regorafenib at its approved dose in the older population.

Protection of trial subjects:

The study was done in accordance with the Declaration of Helsinki (amended 2000) and the International Conference on Harmonization of Technical Requirements of Pharmaceuticals for Human Use (ICH) Note for Guidance on Good Clinical Practice and approved by the appropriate Ethics Committees.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 November 2015
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	France: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	0
From 65 to 84 years	39
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Between January 2016 to April 2017, 43 patients were enrolled in the trial by 25 centers in France.

Pre-assignment

Screening details:

Before enrollement, standard examinations (biological, clinical, ECG) as well as geriatric questionnaires were done. In terms of imaging, abdominal and thoracic computed tomography scan or MRI were also done.

Period 1

Period 1 title	Enrolled patients (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Regorafenib

Arm description:

Regorafenib monotherapy at an initial dose of 160 mg once daily orally (21 days on, 7 days off treatment)

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

Dosage and administration details:

Dose of 160 mg once daily orally (21 days on, 7 days off treatment)

Number of subjects in period 1	Regorafenib
Started	43
Treated patients	42
Completed	42
Not completed	1
Non treated patient	1

Baseline characteristics

Reporting groups

Reporting group title	Enrolled patients

Reporting group description: -

Reporting group values	Enrolled patients	Total	
Number of subjects	43	43	
Age categorical 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)	0	0	
From 65-84 years	39	39	
85 years and over	4	4	
Gender categorical Units: Subjects			
Female	15	15	
Male	28	28	

Subject analysis sets

Subject analysis set title	mITT for efficacy
Subject analysis set type	Full analysis

Subject analysis set description:

The modified intention-to-treat population for efficacy was defined as all patients included in the study who received at least one regorafenib tablet and had imaging or clinical evaluation within 2 months (+1 month) of starting treatment.

Subject analysis set title	mITT Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

mITT population was defined as all patients included in the study who received at least one regorafenib tablet.

Reporting group values	mITT for efficacy	mITT Population	
Number of subjects	35	42	
Age categorical 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)	0	0	
From 65-84 years	32	38	
85 years and over	3	4	
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Regorafenib
Reporting group description:	
Regorafenib monotherapy at an initial dose of 160 mg once daily orally (21 days on, 7 days off treatment)	
Subject analysis set title	mITT for efficacy
Subject analysis set type	Full analysis
Subject analysis set description:	
The modified intention-to-treat population for efficacy was defined as all patients included in the study who received at least one regorafenib tablet and had imaging or clinical evaluation within 2 months (+1 month) of starting treatment.	
Subject analysis set title	mITT Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
mITT population was defined as all patients included in the study who received at least one regorafenib tablet.	

Primary: Disease control rate (DCR) under treatment

End point title	Disease control rate (DCR) under treatment[1]
End point description:	
It was defined as the number of patients with a complete or partial response, or stable disease 2 months post-initiation of study therapy.	
End point type	Primary
End point timeframe:	
At 2 months post-initiation of study therapy.	

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: This study is a single-arm study so no comparison with a another arm.

End point values	mITT for efficacy			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: patients				
Disease Control	11			
No disease control	24			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival
End point description:	
End point type	Secondary

End point timeframe:
until the end of the follow-up or the apperance of progression or death

End point values	mITT Population			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: months				
median (confidence interval 95%)	2.19 (1.97 to 3.29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:
Until the end of the follow-up or death (Whatever the cause)

End point values	mITT Population			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: months				
median (confidence interval 95%)	7.54 (5.52 to 10.58)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs (related and unrelated, expected and unexpected) occurring in the course of the study, from the signature of the informed consent form and until 30 days after the last dose of the study drug were reported by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTC
Dictionary version	4.0

Reporting groups

Reporting group title	mITT population

Reporting group description:

All the patients included in the study having taken at least one dose of regorafenib.

Serious adverse events	mITT population		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 42 (40.48%)		
number of deaths (all causes)	36		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Hypertension			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Haematoma			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular ischemia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Deshydratation			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	mITT population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 42 (50.00%)		
occurrences (all)	21		
Alanine aminotransferase increased			
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	12		
Total Bilirubin increased			
subjects affected / exposed	22 / 42 (52.38%)		
occurrences (all)	22		
Gamma-glutamyltransferase increased			
subjects affected / exposed	31 / 42 (73.81%)		
occurrences (all)	31		
White blood cell count decreased			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Lipase increased			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Neutrophils decreased			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Lymhocytes decreased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Phosphatases Alcalines increased			

subjects affected / exposed	21 / 42 (50.00%)		
occurrences (all)	21		
Platelets decreased			
subjects affected / exposed	20 / 42 (47.62%)		
occurrences (all)	20		
Cardiac disorders			
Hypertension			
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	12		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Dysgueusia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	19 / 42 (45.24%)		
occurrences (all)	19		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	34 / 42 (80.95%)		
occurrences (all)	34		
Pyrexia			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	13		
Diarrhoea			
subjects affected / exposed	17 / 42 (40.48%)		
occurrences (all)	17		
Abdominal pain			

subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		
Stomatitis			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Nausea			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	11		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	18 / 42 (42.86%)		
occurrences (all)	18		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Hypokaliemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Metabolism and nutrition disorders			

Anorexia			
subjects affected / exposed	23 / 42 (54.76%)		
occurrences (all)	23		
Hyperkalaemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Hypoalbuminaemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	15 / 42 (35.71%)		
occurrences (all)	15		
Hypomagnesaemia			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Hyponatremia			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		
Hypophosphataemia			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32334940