

**Clinical trial results:****PHASE II STUDY EVALUATION OF EFFICACY 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 |
| Public contact | Karine Le Malicot - Head of Biostatistics, FEDERATION FRANCOPHONE DE CANCEROLOGIE DIGESTIVE, 33 380393479, karine.le-malicot@u-bourgogne.fr |
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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 main 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 appearance 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 | | | |
| Deshydration | | | |

| | | | |
|---|----------------|--|--|
| 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 | | |
| Lymphocytes decreased | | | |
| subjects affected / exposed | 3 / 42 (7.14%) | | |
| occurrences (all) | 3 | | |
| Phosphatases Alkalines increased | | | |

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