Clinical trial results:
EFFICACY AND SAFETY of aflibercept ASSOCIATED WITH A FOLFIRI CHEMOTHERAPY IN 1ST LINE TREATMENT OF PATIENTS SUFFERING FROM METASTATIC COLORECTAL CANCER
Phase II - single arm - multicenter

Summary

EudraCT number	2013-004081-33
Trial protocol	FR
Global end of trial date	25 September 2018

Results information

Result version number	v1 (current)
This version publication date	24 July 2024
First version publication date	24 July 2024
Summary attachment (see zip file)	FFCD 1302 Princeps Publication (FFCD 1302_Princeps.pdf)

Trial information

Trial identification

Sponsor protocol code	FFCD1302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02181556
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fédération Francophonce de Cancérologie Digestive (FFCD)
Sponsor organisation address	7 bd Jeanne d'ARC, Dijon, France, 21079
Public contact	FFCD, Fédération Francophone de cancérologie digestive, marie.moreau@u-bourgogne.fr
Scientific contact	FFCD, Fédération Francophone de cancérologie digestive, marie.moreau@u-bourgogne.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	25 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2017
Global end of trial reached?	Yes
Global end of trial date	25 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the patients rate without progression or death at 6 months (RECIST version 1.1) according to the investigator

Protection of trial subjects:

The trial was conducted in accordance with the European Directive 2001/20/EC. The investigator obtained the patient's consent for the clinical and the biological studies after providing them adequate information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 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	France: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	21
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was planned to be a 2-steps study. it was stopped at step 1. 41 patients were included by 9 centers between October 2014 and February 2017, including 33 patients from step 1, and 9 patients included in the trial during the 6-month follow-up period. One patient withdrew his consent and was not analyzed

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	40
Number of subjects completed	40

Period 1

Period 1 title	mITT (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open study

Arms

Arm title	Folfiri + Aflibercept

Arm description:

Every 14 days, eligible patients received 4 mg/kg of aflibercept intravenously [IV], over 1 hour, followed immediately by the FOLFIRI regimen (irinotecan 180mg/m2 IV over 90 minutes, with leucovorin 400 mg/m2 IV over 2 hours, followed by 5-FU 400 mg/m2 bolus and 5-FU 2400 mg/m2 continuous infusion over 46 hours). Patients were treated until occurrence of disease progression or unacceptable toxicity according to physician judgment.

Arm type	Experimental
Investigational medicinal product name	FOLFIRI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Every 14 days, FOLFIRI regimen (irinotecan 180mg/m2 IV over 90 minutes, with leucovorin 400 mg/m2 IV over 2 hours, followed by 5-FU 400 mg/m2 bolus and 5-FU 2400 mg/m2 continuous infusion over 46 hours)

Investigational medicinal product name	Aflibercept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Every 14 days, eligible patients received 4 mg/kg of aflibercept intravenously

Number of subjects in period 1	Folfiri + Aflibercept
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	mITT

Reporting group description: -

Reporting group values	mITT	Total	
Number of subjects	40	40	
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)	21	21	
From 65-84 years	19	19	
85 years and over	0	0	
Age continuous Units: years			
median	64.85		
inter-quartile range (Q1-Q3)	61.15 to 71.30	-	
Gender categorical Units: Subjects			
Female	23	23	
Male	17	17	

End points

End points reporting groups

Reporting group title	Folfiri + Aflibercept

Reporting group description:

Every 14 days, eligible patients received 4 mg/kg of aflibercept intravenously [IV], over 1 hour, followed immediately by the FOLFIRI regimen (irinotecan 180mg/m2 IV over 90 minutes, with leucovorin 400 mg/m2 IV over 2 hours, followed by 5-FU 400 mg/m2 bolus and 5-FU 2400 mg/m2 continuous infusion over 46 hours). Patients were treated until occurrence of disease progression or unacceptable toxicity according to physician judgment.

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

Subject analysis set description:

The modified intent-to-treat population wasdefined as all patients included in the study, regardless of eligibility criteria and treatment received, with at least a radiological evaluation during the 6 months of treatment.

Primary: Rate of patients alive and without progression 6 months after inclusion

End point title	Rate of patients alive and without progression 6 months after inclusion[1]

End point description:

Progression wasdefined by :
- Progression assessed by CT scan, according to the RECIST version 1.1 criteria;
- Death from any cause.

Patients without an assessment at 6 months were reviewed according to the following rules:
- If the patient had a later evaluation (7 months or more) and was not progressing at that time, then the patient was considered progression-free at 6 months;
- If the patient presented a documented progression within 2 months of the 6 month assessment then the patient was considered to be progressing at 6 months. If the progression wasdocumented beyond 8 months then the patient was not considered progressive at 6 months;
- If a progression wasdocumented prior to the 6-month assessment, the patient was considered progressive at 6 months.

End point type	Primary

End point timeframe:

6 months after inclusion

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 one-arm study so no statistical inference analysis was done.

End point values	Folfiri + Aflibercept			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: patients				
Patients alive without progression	18			
Patients with progression and/or death	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

It was defined as the time interval between the inclusion date and the date of death (regardless of cause). Patients lost to follow-up or alive at the time of analysis were censored as of the date of last news.

End point type	Secondary

End point timeframe:

30 months

End point values	Folfiri + Aflibercept			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: months				
median (confidence interval 95%)	18.63 (14.69 to 30.65)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected before each cycle od chemotherapy systematically during the whole protocol of treatment

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTC
Dictionary version	4.0

Reporting groups

Reporting group title	mITT patients

Reporting group description: -

Serious adverse events	mITT patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 40 (52.50%)		
number of deaths (all causes)	25		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
infected neoplasm			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Phlebitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar infraction			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile bone narrow aplasia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Small bowel perforation			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal vein thrombosis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			

subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	mITT patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 40 (100.00%)		
Investigations			
ALAT Increased			
subjects affected / exposed	24 / 40 (60.00%)		
occurrences (all)	24		
ASAT Increased			
subjects affected / exposed	25 / 40 (62.50%)		
occurrences (all)	25		
Creatinine increased			
subjects affected / exposed	13 / 40 (32.50%)		
occurrences (all)	13		
GGT increased			
subjects affected / exposed	36 / 40 (90.00%)		
occurrences (all)	36		
Leucopenia			
subjects affected / exposed	20 / 40 (50.00%)		
occurrences (all)	20		
Neutropenia			
subjects affected / exposed	26 / 40 (65.00%)		
occurrences (all)	26		
Weight loss			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	8		

PAL increased subjects affected / exposed occurrences (all) Thrombopenia subjects affected / exposed occurrences (all)	 29 / 40 (72.50%) 29 6 / 40 (15.00%) 6		
Vascular disorders Haemorrhage subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2 20 / 40 (50.00%) 20		
Nervous system disorders Cephalgia subjects affected / exposed occurrences (all) Peripheral neuropathy subjects affected / exposed occurrences (all) Paresthesia subjects affected / exposed occurrences (all)	 4 / 40 (10.00%) 4 2 / 40 (5.00%) 2 6 / 40 (15.00%) 6		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)	 30 / 40 (75.00%) 30		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) Inferior member oedema	 34 / 40 (85.00%) 34 14 / 40 (35.00%) 14		

subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Rectal haemorrhage subjects affected / exposed occurrences (all) Mucositis subjects affected / exposed occurrences (all) Rectal mucositis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 5 / 40 (12.50%) 5 31 / 40 (77.50%) 31 18 / 40 (45.00%) 18 2 / 40 (5.00%) 2 3 / 40 (7.50%) 3 23 / 40 (57.50%) 23 3 / 40 (7.50%) 3 29 / 40 (72.50%) 29 16 / 40 (40.00%) 16		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	 3 / 40 (7.50%) 3 10 / 40 (25.00%) 10		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Cutaneous dryness subjects affected / exposed occurrences (all) Palmo-palmar syndrom subjects affected / exposed occurrences (all)	 14 / 40 (35.00%) 14 3 / 40 (7.50%) 3 9 / 40 (22.50%) 9		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	 13 / 40 (32.50%) 13		
Musculoskeletal and connective tissue disorders Dorsalgia subjects affected / exposed occurrences (all)	 4 / 40 (10.00%) 4		
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Hypoalbuminemia subjects affected / exposed occurrences (all) Hypocalcemia subjects affected / exposed occurrences (all) Hypokaliemia	 12 / 40 (30.00%) 12 3 / 40 (7.50%) 3 4 / 40 (10.00%) 4		

subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Hyponatremia			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		

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? Yes

Date	Interruption	Restart date
03 May 2017	Inclusions were stopped at the interim analysis because the combination was considered as non-efficient	-

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32921581