Clinical trial results:
PHASE II RANDOMIZED TRIAL EVALUATING AFLIBERCEPT ASSOCIATED WITH SCHEME LV5FU2 AS FIRST LINE TREATMENT OF NON-RESECTABLE METASTATIC COLORECTAL CANCERS

Summary

EudraCT number	2014-001837-10
Trial protocol	FR
Global end of trial date	15 June 2021

Results information

Result version number	v1 (current)
This version publication date	06 July 2025
First version publication date	06 July 2025

Trial information

Trial identification

Sponsor protocol code	PRODIGE25

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02384759
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fédération Francophone de Cancérologie Digestive
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	28 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2021
Global end of trial reached?	Yes
Global end of trial date	15 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Proportion of patients alive and without radiological progression within 6 months (RECIST 1.1) according to the investigator

Protection of trial subjects:

This trial was conducted in accordance with the New European Directive 2001/20/EC. The investigator undertook to obtain the patient's consent for the clinical and biological studies in writing, after providing adequate information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 May 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: 117
Worldwide total number of subjects	117
EEA total number of subjects	117

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	94
85 years and over	23

Subject disposition

Recruitment

Recruitment details:

Between May 2015 and September 2020, 117/118 patients (pts) were randomized by 33 centers with 59 in arm A (5FU-aflibercept) and 58 in arm B (5FU alone).

Pre-assignment

Screening details:

Main eligibility criteria were histologically proven non-resectable metastatic rectal or colon adenocarcinoma, not pre-treated for metastatic disease, patients' age ≥ 65,WHO performance status (PS) ≤ 2, and central determination of germline TS-5'UTR genotype on blood DNA for stratification

Period 1

Period 1 title	Baseline period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Aflibercept + LV5FU2s

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LV5FU2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

LV5FU2 simplified every 2 weeks: folinic acid 400 mg/m2 IV over 90 min, then 5FU 400 mg/m2 IV bolus at D1, followed by continuous infusion of 5FU 2400 mg/m2 over 46 h.

Arm title	Arm B : LVFU2s

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	LV5FU2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

LV5FU2 simplified every 2 weeks: folinic acid 400 mg/m2 IV over 90 min, then 5FU 400 mg/m2 IV bolus at D1, followed by continuous infusion of 5FU 2400 mg/m2 over 46 h.

Number of subjects in period 1	Arm A: Aflibercept + LV5FU2s	Arm B : LVFU2s
Started	59	58
Completed	56	56
Not completed	3	2
Alteration of their conditions	3	2

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Aflibercept + LV5FU2s

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LV5FU2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

LV5FU2 simplified every 2 weeks: folinic acid 400 mg/m2 IV over 90 min, then 5FU 400 mg/m2 IV bolus at D1, followed by continuous infusion of 5FU 2400 mg/m2 over 46 h.

Arm title	Arm B : LVFU2s

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	LV5FU2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

LV5FU2 simplified every 2 weeks: folinic acid 400 mg/m2 IV over 90 min, then 5FU 400 mg/m2 IV bolus at D1, followed by continuous infusion of 5FU 2400 mg/m2 over 46 h.

Number of subjects in period 2	Arm A: Aflibercept + LV5FU2s	Arm B : LVFU2s
Started	56	56
Completed	56	56

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Aflibercept + LV5FU2s
Reporting group description: -	
Reporting group title	Arm B : LVFU2s
Reporting group description: -	

Reporting group values	Arm A: Aflibercept + LV5FU2s	Arm B : LVFU2s	Total
Number of subjects	59	58	117
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	48	46	94
85 years and over	11	12	23
Age continuous Units: years			
median	81	80.9	
inter-quartile range (Q1-Q3)	76.9 to 84	78.3 to 84.4	-
Gender categorical Units: Subjects			
Female	22	23	45
Male	37	35	72

End points

End points reporting groups

Reporting group title	Arm A: Aflibercept + LV5FU2s
Reporting group description: -	
Reporting group title	Arm B : LVFU2s
Reporting group description: -	
Reporting group title	Arm A: Aflibercept + LV5FU2s
Reporting group description: -	
Reporting group title	Arm B : LVFU2s
Reporting group description: -	

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:

The primary endpoint of this trial was the rate of patients alive and progression-free 6 months (+/- 15 days) after randomization. Progression was assessed by the investigator according to RECIST 1.1 criteria, on the basis of imaging examinations performed every 8 weeks, even in the event of deferred treatments.
Clinical progressions not confirmed on imaging were not included in the primary endpoint.
Patients with progression on imaging examinations prior to 6 months were considered as having progressed at 6 months.

End point type	Primary

End point timeframe:

6 months after randomization

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: The study was a non-comparative study that's why no statistical analysis was done.

End point values	Arm A: Aflibercept + LV5FU2s	Arm B : LVFU2s		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: patients				
Patients alive without progression at 6 months	30	30		
Patients with progression or death at 6 months	26	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Best response under treatment

End point title	Best response under treatment

End point description:

Response was assessed on the basis of all patients' radiological examinations according to RECIST 1.1 criteria, as determined by the investigator during protocol treatment. Any scans performed after discontinuation of protocol therapy (within 2 months) was taken into account if no second-line therapy started.

End point type	Secondary

End point timeframe:

From randomization until the end of the treatment

End point values	Arm A: Aflibercept + LV5FU2s	Arm B : LVFU2s		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: patients				
Complete response	0	0		
Partial response	14	22		
Stability	30	26		
Progression	9	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

It was defined by the time between the date of randomization and the date of death (from any cause); Alive patients were censored at the date of last news .

End point type	Secondary

End point timeframe:

30 months

End point values	Arm A: Aflibercept + LV5FU2s	Arm B : LVFU2s		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	56		
Units: months				
median (confidence interval 95%)	21.85 (12.1 to 25.0)	25.07 (19.8 to 31.9)		

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	Bras A: LV5FU2s + Aflibercept
Reporting group description: -	
Reporting group title	Arm B: LVF5U2s

Reporting group description: -

Serious adverse events	Bras A: LV5FU2s + Aflibercept	Arm B: LVF5U2s	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 56 (46.43%)	14 / 56 (25.00%)	
number of deaths (all causes)	37	36	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 56 (5.36%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			

subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Perineal haematoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	5 / 56 (8.93%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	4 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	2 / 56 (3.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood electrolytes abnormal			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Fall			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Intracardiac thrombus			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amnesia			

subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 56 (3.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 56 (1.79%)	2 / 56 (3.57%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	5 / 56 (8.93%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	5 / 56 (8.93%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	2 / 56 (3.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	2 / 56 (3.57%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 56 (3.57%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Bras A: LV5FU2s + Aflibercept	Arm B: LVF5U2s	
Total subjects affected by non-serious adverse events subjects affected / exposed	55 / 56 (98.21%)	56 / 56 (100.00%)	
Investigations			
ALAT increase			
subjects affected / exposed	16 / 56 (28.57%)	14 / 56 (25.00%)	
occurrences (all)	16	14	
ASAT Increase			
subjects affected / exposed	21 / 56 (37.50%)	15 / 56 (26.79%)	
occurrences (all)	21	15	
Bilirunin increase			
subjects affected / exposed	13 / 56 (23.21%)	11 / 56 (19.64%)	
occurrences (all)	13	11	
Creatinin increase			
subjects affected / exposed	23 / 56 (41.07%)	21 / 56 (37.50%)	
occurrences (all)	23	21	
GGT Increase			
subjects affected / exposed	38 / 56 (67.86%)	31 / 56 (55.36%)	
occurrences (all)	38	31	
Leucopenia			
subjects affected / exposed	9 / 56 (16.07%)	14 / 56 (25.00%)	
occurrences (all)	9	14	
Neutropenia			
subjects affected / exposed	9 / 56 (16.07%)	16 / 56 (28.57%)	
occurrences (all)	9	16	
Lymphopenia			
subjects affected / exposed	7 / 56 (12.50%)	16 / 56 (28.57%)	
occurrences (all)	7	16	
PAL increase			
subjects affected / exposed	29 / 56 (51.79%)	24 / 56 (42.86%)	
occurrences (all)	29	24	
Weight loss			
subjects affected / exposed	10 / 56 (17.86%)	5 / 56 (8.93%)	
occurrences (all)	10	5	
Thombopenia			

subjects affected / exposed	15 / 56 (26.79%)	16 / 56 (28.57%)	
occurrences (all)	15	16	
Hypoalbuminemia			
subjects affected / exposed	3 / 56 (5.36%)	4 / 56 (7.14%)	
occurrences (all)	3	4	
Nervous system disorders			
Cephalgia			
subjects affected / exposed	6 / 56 (10.71%)	2 / 56 (3.57%)	
occurrences (all)	6	2	
Dysgueusia			
subjects affected / exposed	5 / 56 (8.93%)	6 / 56 (10.71%)	
occurrences (all)	5	6	
Neuropathy			
subjects affected / exposed	6 / 56 (10.71%)	2 / 56 (3.57%)	
occurrences (all)	6	2	
Paresthesia			
subjects affected / exposed	4 / 56 (7.14%)	4 / 56 (7.14%)	
occurrences (all)	4	4	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	36 / 56 (64.29%)	43 / 56 (76.79%)	
occurrences (all)	36	43	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	48 / 56 (85.71%)	44 / 56 (78.57%)	
occurrences (all)	48	44	
Fever			
subjects affected / exposed	7 / 56 (12.50%)	8 / 56 (14.29%)	
occurrences (all)	7	8	
Edema of the lower limbs			
subjects affected / exposed	7 / 56 (12.50%)	6 / 56 (10.71%)	
occurrences (all)	7	6	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 56 (5.36%)	7 / 56 (12.50%)	
occurrences (all)	3	7	

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	15 / 56 (26.79%)	18 / 56 (32.14%)	
occurrences (all)	15	18	
Diarrhoea			
subjects affected / exposed	30 / 56 (53.57%)	29 / 56 (51.79%)	
occurrences (all)	30	29	
Abdominal pain			
subjects affected / exposed	15 / 56 (26.79%)	12 / 56 (21.43%)	
occurrences (all)	15	12	
Gastroesophageal reflux disease			
subjects affected / exposed	4 / 56 (7.14%)	2 / 56 (3.57%)	
occurrences (all)	4	2	
Mucositis			
subjects affected / exposed	24 / 56 (42.86%)	25 / 56 (44.64%)	
occurrences (all)	24	25	
Nausea			
subjects affected / exposed	18 / 56 (32.14%)	23 / 56 (41.07%)	
occurrences (all)	18	23	
Vomiting			
subjects affected / exposed	7 / 56 (12.50%)	9 / 56 (16.07%)	
occurrences (all)	7	9	
Respiratory, thoracic and mediastinal disorders			
Voice alteration			
subjects affected / exposed	10 / 56 (17.86%)	2 / 56 (3.57%)	
occurrences (all)	10	2	
Dyspnoea			
subjects affected / exposed	4 / 56 (7.14%)	6 / 56 (10.71%)	
occurrences (all)	4	6	
Epistaxis			
subjects affected / exposed	14 / 56 (25.00%)	9 / 56 (16.07%)	
occurrences (all)	14	9	
Cough			
subjects affected / exposed	7 / 56 (12.50%)	3 / 56 (5.36%)	
occurrences (all)	7	3	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	6 / 56 (10.71%)	8 / 56 (14.29%)	
occurrences (all)	6	8	
Dry skin			
subjects affected / exposed	7 / 56 (12.50%)	13 / 56 (23.21%)	
occurrences (all)	7	13	
Palmar erythrodysesthesia syndrome			
subjects affected / exposed	18 / 56 (32.14%)	13 / 56 (23.21%)	
occurrences (all)	18	13	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	28 / 56 (50.00%)	7 / 56 (12.50%)	
occurrences (all)	28	7	
Musculoskeletal and connective tissue disorders			
Dorsalgia			
subjects affected / exposed	3 / 56 (5.36%)	8 / 56 (14.29%)	
occurrences (all)	3	8	
Parietal thoracic painn			
subjects affected / exposed	4 / 56 (7.14%)	3 / 56 (5.36%)	
occurrences (all)	4	3	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	30 / 56 (53.57%)	18 / 56 (32.14%)	
occurrences (all)	30	18	
Hyperglycemia			
subjects affected / exposed	3 / 56 (5.36%)	5 / 56 (8.93%)	
occurrences (all)	3	5	
Hyperkaliemia			
subjects affected / exposed	18 / 56 (32.14%)	5 / 56 (8.93%)	
occurrences (all)	18	5	
Hyponatremia			
subjects affected / exposed	9 / 56 (16.07%)	5 / 56 (8.93%)	
occurrences (all)	9	5	

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/38672597