Clinical trial results:
Everolimus After (Chemo)Embolization for Liver Metastases From Digestive Endocrine Tumors (EVACEL)

Summary

EudraCT number	2012-002224-32
Trial protocol	FR
Global end of trial date	12 October 2018

Results information

Result version number	v1 (current)
This version publication date	13 July 2025
First version publication date	13 July 2025

Trial information

Trial identification

Sponsor protocol code	FFCD 1104

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01678664
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fédération Francophone de Cancérologie Digestive (FFCD)
Sponsor organisation address	7 Boulevard Jeanne d'Arc, BP 87900, Dijon, France, 21079
Public contact	Marie Moreau, Fédération Francophone de Cancérologie Digestive, marie.moreaut@u-bourgogne.fr
Scientific contact	Marie Moreau, Fédération Francophone de Cancérologie Digestive (FFCD), +33 0755676632, 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	27 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 August 2018
Global end of trial reached?	Yes
Global end of trial date	12 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary end-point of this study was the hepatic progression-free survival rate (based on the central assessment) as defined by RECIST v1.1 at 24 months after treatment

Protection of trial subjects:

This protocol was authorised by the French Medicines Agency (Agence Francaise de Securite Sanitaire des Produits de Sante´) on 29 June 2012.
(A120657-42), and the trial was registered on the clinicaltrials.gov website (NCT01678664). The study complies with the Declaration of Helsinki rules and the principles of Good Clinical Practice guidelines. All patients gave written informed consent for participation in this trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2012
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: 74
Worldwide total number of subjects	74
EEA total number of subjects	74

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)	32
From 65 to 84 years	41

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 74 patients were included between January 2013 and March 2016.

Pre-assignment

Screening details:

Before enrollement, standard examinations (biological, clinical, TDM, ECG) were done. Inclusion and non inclusion criteria had to be met.

Period 1

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

Blinding implementation details:

Not blinding

Arms

Arm title	Embolization or chemoembolization plus everolimus

Arm description:

The hepatic arterial embolisation therapy (HAET) including hepatic arterial embolisation (HAE) by particulate embolisation of the hepatic arterial branches feeding the targeted liver metastases or transarterial chemoembolisation (TACE) using a mixture of lipiodol with either doxorubicin (50 mg/m2, up to a target of total dose of 100 mg) or streptozotocin (1500 mg/m2) followed by particulate embolisation using either gelatin sponge particles or spherical embolics up to stasis. The treatment plan allowed for a maximum of two procedures. Everolimus (10 mg/day) was started 7 days after the HAET and once hepatic toxicity had improved to grade <= I. The treatment had to start <=30 days after HAET.

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

Dosage and administration details:

10 mg/day (either 1 tablet of 10mg or 2 tablets of 5mg) during 24 months or until progression disease. started 7 days after the HAET and once hepatic toxicity had improved to grade <= I. The treatment had to start <=30 days after HAET. The duration of everolimus treatment was 24 months after the first procedure in the absence of unacceptable toxicity.

Investigational medicinal product name	Embolization
Investigational medicinal product code	
Other name	spheric particules of 100 to 500 µm
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarterial use

Dosage and administration details:

2 sessions embolization with spheric particle

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection

Routes of administration	Intraarterial use

Dosage and administration details:

2 sessions chemoembolization with 10 ml of lipiodol and either 100 mg of doxorubicin or streptozotocin (1500 mg/m2)
(reconstituted in 5 ml or the smallest possible volume of liquid).

Investigational medicinal product name	Lipiodol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarterial use

Dosage and administration details:

2 sessions chemoembolization with 10 ml of lipiodol and either 100 mg of doxorubicin or streptozotocin (1500 mg/m2)
(reconstituted in 5 ml or the smallest possible volume of liquid).

Investigational medicinal product name	Streptozotocin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarterial use

Dosage and administration details:

2 sessions chemoembolization with 10 ml of lipiodol and either 100 mg of doxorubicin or streptozotocin (1500 mg/m2)
(reconstituted in 5 ml or the smallest possible volume of liquid).

Number of subjects in period 1	Embolization or chemoembolization plus everolimus
Started	74
Completed	13
Not completed	61
Physician decision	7
Not recovered at day 30 from HAET	3
Disease progression	21
Adverse event, non-fatal	24
Unknown	4
Patient choice	2

Baseline characteristics

Reporting groups

Reporting group title	Baseline period

Reporting group description: -

Reporting group values	Baseline period	Total	
Number of subjects	74	74	
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)	32	32	
From 65-84 years	41	41	
85 years and over	1	1	
Age continuous Units: years			
median	66		
full range (min-max)	43 to 86	-	
Gender categorical Units: Subjects			
Female	31	31	
Male	43	43	
Primary site Units: Subjects			
Small bowel	64	64	
Caecum and colon	3	3	
Rectum	2	2	
Stomach	2	2	
Unknown	3	3	
Performance status Units: Subjects			
PS 0	48	48	
PS 1	25	25	
PS 2	1	1	
Tumor grade Units: Subjects			
Grade I	32	32	
Grade II	42	42	
Median liver tumour burden Units: Subjects			
< 25%	29	29	
25% - 50%	24	24	

50% - 75%	14	14	
> 75%	7	7	
Disease progression at study entry			
by RECIST criteria			
Units: Subjects			
Yes	74	74	
Previous carcinoid syndrome Units: Subjects			
Yes	32	32	
No	42	42	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients included in the trial, whatever the eligibility criteria are and the treatment received.

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

Subject analysis set description:

Modified intention-to-treat population is defined as the ITT population who have received at least one (chemo) embolization and at least one dose of everolimus.

Reporting group values	ITT	mITT	
Number of subjects	74	67	
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)	32	29	
From 65-84 years	41	37	
85 years and over	1	1	
Age continuous Units: years			
median	66	66	
full range (min-max)	43 to 86	43 to 86	
Gender categorical Units: Subjects			
Female	31	28	
Male	43	39	
Primary site Units: Subjects			
Small bowel	64		
Caecum and colon	3		
Rectum	2		
Stomach	2		

Unknown	3		
Performance status Units: Subjects			
PS 0	48		
PS 1	25		
PS 2	1		
Tumor grade Units: Subjects			
Grade I	32		
Grade II	42		
Median liver tumour burden Units: Subjects			
< 25%	29		
25% - 50%	24		
50% - 75%	14		
> 75%	7		
Disease progression at study entry			
by RECIST criteria			
Units: Subjects			
Yes	74		
Previous carcinoid syndrome Units: Subjects			
Yes	32		
No	42		

End points

End points reporting groups

Reporting group title	Embolization or chemoembolization plus everolimus

Reporting group description:

The hepatic arterial embolisation therapy (HAET) including hepatic arterial embolisation (HAE) by particulate embolisation of the hepatic arterial branches feeding the targeted liver metastases or transarterial chemoembolisation (TACE) using a mixture of lipiodol with either doxorubicin (50 mg/m2, up to a target of total dose of 100 mg) or streptozotocin (1500 mg/m2) followed by particulate embolisation using either gelatin sponge particles or spherical embolics up to stasis. The treatment plan allowed for a maximum of two procedures. Everolimus (10 mg/day) was started 7 days after the HAET and once hepatic toxicity had improved to grade <= I. The treatment had to start <=30 days after HAET.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients included in the trial, whatever the eligibility criteria are and the treatment received.

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

Subject analysis set description:

Modified intention-to-treat population is defined as the ITT population who have received at least one (chemo) embolization and at least one dose of everolimus.

Primary: Hepatic Progression-free survival rate at 24 months (24 months hPFS)

End point title	Hepatic Progression-free survival rate at 24 months (24 months hPFS)[1]

End point description:

The primary end-point of this study was the hPFS rate (based on the central assessment) as defined by RECIST v1.1 (including death considered as progression) at 24 months after treatment.
In the 67 mITT patients : If 31 or more patients are alive without hepatic progression at 24 months, we conclude that the treatment is effective.

End point type	Primary

End point timeframe:

at 24 months after treatment.

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 is a non-comparative study, so there are no inferential statistics.

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	67			
Units: patients				
Yes	22			
No	45			

Statistical analyses

No statistical analyses for this end point

Secondary: Hepatic progression-free survival (hPFS)

End point title	Hepatic progression-free survival (hPFS)

End point description:

Progression-free survival rate (PFS) (based on the investigator) according to RECIST v1.1 according to RECIST v1.1 will be defined as the time from the date of inclusion to the date of hepatic progression or death (due to any cause). For patients who are alive with no hepatic progression, it will be defines as the time from the date of inclusion and the date of the last tumor assessment.

End point type	Secondary

End point timeframe:

until the date of first hepatic progression or death from any cause whichever came first, assessed up to 3 years

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	74			
Units: months				
median (confidence interval 95%)	18.5 (14.0 to 22.8)			

Attachments (see zip file)	PFS and hPFS/Fig 1a.tif

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was defined as the time from the date of inclusion to the date of death, regardless of the cause of death, or the date of last contact for patients who are alive.

End point type	Secondary

End point timeframe:

Until the end of the follow-up or death (Whatever the cause)

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	74			
Units: months				
median (confidence interval 95%)	51.0 (33.0 to 60.3)			

Attachments (see zip file)	OS/Fig 1b.tif

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

Progression-free survival rate was defined as the time from the date of inclusion to the date of disease progression (hepatic or not) evaluated by RECIST V1.1 criteria or death (due to any cause) or the date of the last news for alive patients

End point type	Secondary

End point timeframe:

until the date of first progression (clinical or radiological) or death from any cause whichever came first, assessed up to 3 years

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	74			
Units: months				
median (confidence interval 95%)	16.9 (12.6 to 22.4)			

Attachments (see zip file)	PFS and hPFS/Fig 1a.tif

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response

End point title	Objective response

End point description:

Objective response (Complete or partial response) evaluated by investigator and RECIST v1.1 criteria

End point type	Secondary

End point timeframe:

during treatment

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	74			
Units: patients				
Yes	40			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected every 3 months between 2 consultations until the end of the treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTC
Dictionary version	4.0

Reporting groups

Reporting group title	mITT

Reporting group description:

All the patients included in the study having at least one (chemo) embolization and taken at least one dose of everolimus.

Serious adverse events	mITT		
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 67 (52.24%)		
number of deaths (all causes)	32		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour compression			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Shock			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vena cava thrombosis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Chest pain			

subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Right ventricular failure			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Anemia			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Asthenia				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	6 / 67 (8.96%)			
occurrences causally related to treatment / all	2 / 6			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Nausea				
subjects affected / exposed	2 / 67 (2.99%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 67 (4.48%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ascite				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	5 / 67 (7.46%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	2 / 67 (2.99%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	1 / 67 (1.49%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				

Cholecystitis			
subjects affected / exposed	7 / 67 (10.45%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic cirrhosis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatic necrosis			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatitis alcoholic			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute prerenal failure			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			

subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Parotitis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abscess			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
staphylococcal sepsis			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Deshydration			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			

subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	2 / 67 (2.99%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatremia			
subjects affected / exposed	1 / 67 (1.49%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	3 / 67 (4.48%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	mITT		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 67 (100.00%)		
Vascular disorders			
Flush			
subjects affected / exposed	6 / 67 (8.96%)		
occurrences (all)	6		
Thromboembolic event			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	4		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	59 / 67 (88.06%) 59		
Fever subjects affected / exposed occurrences (all)	25 / 67 (37.31%) 25		
Oedema of the limbs subjects affected / exposed occurrences (all)	26 / 67 (38.81%) 26		
Immune system disorders Allergic reaction subjects affected / exposed occurrences (all)	4 / 67 (5.97%) 4		
Respiratory, thoracic and mediastinal disorders Dyspnea subjects affected / exposed occurrences (all)	15 / 67 (22.39%) 15		
Epistaxis subjects affected / exposed occurrences (all)	7 / 67 (10.45%) 7		
Pneumonitis subjects affected / exposed occurrences (all)	7 / 67 (10.45%) 7		
Cough subjects affected / exposed occurrences (all)	11 / 67 (16.42%) 11		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	4 / 67 (5.97%) 4		
Investigations High cholesterol subjects affected / exposed occurrences (all)	37 / 67 (55.22%) 37		
Lymphocyte count decreased			

subjects affected / exposed occurrences (all) Weight loss subjects affected / exposed occurrences (all)	9 / 67 (13.43%) 9 8 / 67 (11.94%) 8		
Nervous system disorders Dysgueusia subjects affected / exposed occurrences (all)	 8 / 67 (11.94%) 8		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all) Neutrophils decreased subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 61 / 67 (91.04%) 61 38 / 67 (56.72%) 38 21 / 67 (31.34%) 21 21 / 67 (31.34%) 21		
Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Oral mucositis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting	 47 / 67 (70.15%) 47 27 / 67 (40.30%) 27 32 / 67 (47.76%) 32 25 / 67 (37.31%) 25		

subjects affected / exposed	22 / 67 (32.84%)		
occurrences (all)	22		
Hepatobiliary disorders			
Alanine aminotransferase increased			
subjects affected / exposed	45 / 67 (67.16%)		
occurrences (all)	45		
Aspartate aminotransferase increased			
subjects affected / exposed	53 / 67 (79.10%)		
occurrences (all)	53		
Bilirubin increased			
subjects affected / exposed	20 / 67 (29.85%)		
occurrences (all)	20		
Creatinine increased			
subjects affected / exposed	25 / 67 (37.31%)		
occurrences (all)	25		
Gamma-glutamyltransferase increased			
subjects affected / exposed	60 / 67 (89.55%)		
occurrences (all)	60		
Hyperuricemia			
subjects affected / exposed	11 / 67 (16.42%)		
occurrences (all)	11		
Alkaline phosphatase increased			
subjects affected / exposed	57 / 67 (85.07%)		
occurrences (all)	57		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 67 (14.93%)		
occurrences (all)	10		
Maculopapular rash			
subjects affected / exposed	9 / 67 (13.43%)		
occurrences (all)	9		
Nail loss			
subjects affected / exposed	4 / 67 (5.97%)		
occurrences (all)	4		
Pruritus			

subjects affected / exposed	6 / 67 (8.96%)		
occurrences (all)	6		
Dry skin			
subjects affected / exposed	8 / 67 (11.94%)		
occurrences (all)	8		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 67 (8.96%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	8 / 67 (11.94%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	21 / 67 (31.34%)		
occurrences (all)	21		
Hyperglycemia			
subjects affected / exposed	51 / 67 (76.12%)		
occurrences (all)	51		
Hyperkaliemia			
subjects affected / exposed	5 / 67 (7.46%)		
occurrences (all)	5		
Hypertriglyceridemia			
subjects affected / exposed	38 / 67 (56.72%)		
occurrences (all)	38		
Hypoalbuminemia			
subjects affected / exposed	11 / 67 (16.42%)		
occurrences (all)	11		
Hypocalcemia			
subjects affected / exposed	26 / 67 (38.81%)		
occurrences (all)	26		
Hypokaliemia			
subjects affected / exposed	11 / 67 (16.42%)		
occurrences (all)	11		
Hypomagnesemia			

subjects affected / exposed	14 / 67 (20.90%)		
occurrences (all)	14		
Hyponatremia			
subjects affected / exposed	23 / 67 (34.33%)		
occurrences (all)	23		
Hypophosphatemia			
subjects affected / exposed	22 / 67 (32.84%)		
occurrences (all)	22		

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/31678771