Clinical trial results:
Essai randomisé en double aveugle de phase II/III évaluant la chimioembolisation combinée au sunitinib ou à un placebo chez des patients atteints de carcinome hépatocellulaire (SATURNE)

Summary

EudraCT number	2009-017064-16
Trial protocol	FR
Global end of trial date	18 June 2021

Results information

Result version number	v1 (current)
This version publication date	27 August 2022
First version publication date	27 August 2022

Trial information

Trial identification

Sponsor protocol code	PRODIGE16

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01164202
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, Fédération Francophone de Cancérologie Digestive (FFCD), 33 380393479, karine.le-malicot@u-bourgogne.fr
Scientific contact	Karine Le Malicot Head of Biostatistics, Fédération Francophone de Cancérologie Digestive (FFCD), 33 380393479, karine.le-malicot@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	15 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 February 2015
Global end of trial reached?	Yes
Global end of trial date	18 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We evaluated the effects of sunitinib plus doxorubicin-TACE on bleeding or liver failure. Patients with HCC were included in this randomized, double-blind study. They received one to three TACE plus either sunitinib or placebo four weeks out of six for one year. The occurrence of severe bleeding or liver failure was assessed during theweek after the TACE. The safety and survival outcomes were evaluated.

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	20 May 2011
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: 78
Worldwide total number of subjects	78
EEA total number of subjects	78

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)	33

From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From May 2011 to May 2014, 78 patients were randomizedin the study, 39 in each group by 17 french centers.

Pre-assignment

Screening details:

After checking the inclusion and non-inclusion criteria, patients were randomized to the protocol. Patient were eligible if they have an HCC diagnosed by imag-ing or histology, with Child-Pugh score A, WHO score ≤ 2, not suitable for surgery resection or radiofrequency ablation,with no extra hepatic disease and portal vein thrombosis.

Period 1

Period 1 title	Randomized Patients (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	TACE + Sunitinib

Arm description:

Transarterial chemoembolization: Chemoembolisation + Sunitinib (SUTENT®) 37.5 mg/d (3 cps of 12.5 mg) orally 4 weeks over 6 (4 weeks of treatment followed by 2 weeks without treatment) during 1 year

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

Dosage and administration details:

Sunitinib (SUTENT®, Pfizer) 37.5 mg/d (3 tablets of 12.5 mg per day) treatment or matching placebo treatment (3tablets per day) were administered orally 7—15 days before first TACE, then 4 weeks over 6 (including 2 weeks with no treatment) during one year

Arm title	TACE + Placebo

Arm description:

Transarterial chemoembolization: Chemoembolisation +
Placebo 3cps/days 4 weeks over 6 during 1 year

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

Dosage and administration details:

Matching placebo treatment (3 tablets per day) were administered orally 7—15 days before first TACE, then 4 weeks over 6 (including 2 weeks with no treatment) during one year

Number of subjects in period 1	TACE + Sunitinib	TACE + Placebo
Started	39	39
Analysis population (mITT)	36	34
Completed	36	34
Not completed	3	5
No TACE	3	5

Baseline characteristics

Reporting groups	
Reporting group title	TACE + Sunitinib

Reporting group description:

Transarterial chemoembolization: Chemoembolisation + Sunitinib (SUTENT®) 37.5 mg/d (3 cps of 12.5 mg) orally 4 weeks over 6 (4 weeks of treatment followed by 2 weeks without treatment) during 1 year

Reporting group title	TACE + Placebo

Reporting group description:

Transarterial chemoembolization: Chemoembolisation + Placebo 3cps/days 4 weeks over 6 during 1 year

Reporting group values	TACE + Sunitinib	TACE + Placebo	Total
Number of subjects	39	39	78
Age categorical			
Age at baseline			
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)	18	15	33
From 65-84 years	21	24	45
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	64.7	66.7	
standard deviation	± 8.20	± 8.5	-
Gender categorical			
Units: Subjects			
Female	3	4	7
Male	36	35	71
CHILD-PUGH			
Units: Subjects			
Classe A-5	27	24	51
Classe A-6	9	13	22
Classe B	2	2	4
Classe C	0	0	0
Missing Data	1	0	1
HCC Disease			
Units: Subjects			
Unilobar	13	23	36
Bi-lobar	26	15	41

Missing Data	0	1	1

Subject analysis sets

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

Subject analysis set description:

The modified IIT population wasdefined as all patients included in the study, regardless of eligibility criteria and who had at least one chemoembolization whatever the dose of oral treatment received

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population was defined as the ITT population who received at least one day of treatment with sunitinib/placebo (no constraints on chemoembolization).

Reporting group values	mITT	Safety population	
Number of subjects	70	77	
Age categorical			
Age at baseline			
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)	29	33	
From 65-84 years	41	44	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	65.9	65.7	
standard deviation	± 8.6	± 8.4	
Gender categorical			
Units: Subjects			
Female	6	7	
Male	64	70	
CHILD-PUGH			
Units: Subjects			
Classe A-5	47	51	
Classe A-6	19	21	
Classe B	3	4	
Classe C	0	0	
Missing Data	1	1	
HCC Disease			
Units: Subjects			
Unilobar	31	35	
Bi-lobar	39	41	

Missing Data	0	1	

End points

End points reporting groups

Reporting group title	TACE + Sunitinib

Reporting group description:

Transarterial chemoembolization: Chemoembolisation + Sunitinib (SUTENT®) 37.5 mg/d (3 cps of 12.5 mg) orally 4 weeks over 6 (4 weeks of treatment followed by 2 weeks without treatment) during 1 year

Reporting group title	TACE + Placebo

Reporting group description:

Transarterial chemoembolization: Chemoembolisation +
Placebo 3cps/days 4 weeks over 6 during 1 year

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

Subject analysis set description:

The modified IIT population wasdefined as all patients included in the study, regardless of eligibility criteria and who had at least one chemoembolization whatever the dose of oral treatment received

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population was defined as the ITT population who received at least one day of treatment with sunitinib/placebo (no constraints on chemoembolization).

Primary: Severe bleeding and/or liver failure

End point title	Severe bleeding and/or liver failure[1]

End point description:

A severe bleeding was defined as either any bleeding(inguinal, tumoral, gastro-intestinal) requiring a local treat-ment (other than inguinal compression), or any bleedingrequiring a systemic treatment (e.g. blood transfusion), oran inguinal bleeding during more than 24 hours. A severeliver failure was defined as the occurrence of any of thefollowing complications: hepatic encephalopathy, onset ofascites, increase of bilirubin level > 10 mg/L, decrease ofprothrombin rate ≤ 50%.

End point type	Primary

End point timeframe:

Up to 7 days following the TACE

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: PRODIGE 16 , Phase II is a randomized on comparative study so no comparison is provided

End point values	TACE + Sunitinib	TACE + Placebo	mITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	36	34	70	
Units: subjects				
Severe bleeding and/or liver failure	1	2	3	
No severe bleeding and no liver failure	35	32	67	

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:

From randomization until the date of first progression (clinical or radiological) or death from any cause whichever came first

End point values	TACE + Sunitinib	TACE + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	38		
Units: months				
median (confidence interval 95%)	9.05 (5.81 to 11.63)	5.51 (4.14 to 7.79)		

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:

From randomization until death or last news for alive patients

End point values	TACE + Sunitinib	TACE + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	38		
Units: months				
median (confidence interval 95%)	25 (13.5 to 36.8)	20.5 (15.1 to 30.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to the end of treatment, on the average of 9 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI-CTC
Dictionary version	4.0

Reporting groups	
Reporting group title	TACE + Sunitinib
Reporting group description: -	
Reporting group title	TACE + Placebo
Reporting group description: -	

Serious adverse events	TACE + Sunitinib	TACE + Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 39 (35.90%)	13 / 38 (34.21%)	
number of deaths (all causes)	32	30	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basocellular carcinoma			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HCC carcinoma			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombo-embolic event			

subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Abdominal pain			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 39 (7.69%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemoptysis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Hallucinations			

subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychosis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Decompensation			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Platelets decreased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Acute Pancreatitis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorexia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Black stools			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver failure			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Liver abscess			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kystes			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 39 (0.00%)	3 / 38 (7.89%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TACE + Sunitinib	TACE + Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 39 (100.00%)	38 / 38 (100.00%)	
Vascular disorders			
Thrombo-embolic event			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Hypertension			

subjects affected / exposed	10 / 39 (25.64%)	16 / 38 (42.11%)	
occurrences (all)	10	16	
General disorders and administration site conditions			
Global health alteration			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Cramps			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Inferior Members oedema			
subjects affected / exposed	5 / 39 (12.82%)	4 / 38 (10.53%)	
occurrences (all)	5	4	
Arthralgia			
subjects affected / exposed	0 / 39 (0.00%)	3 / 38 (7.89%)	
occurrences (all)	0	3	
Headache			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences (all)	3	2	
Pain			
subjects affected / exposed	2 / 39 (5.13%)	5 / 38 (13.16%)	
occurrences (all)	2	5	
Back pain			
subjects affected / exposed	3 / 39 (7.69%)	0 / 38 (0.00%)	
occurrences (all)	3	0	
Asthenia			
subjects affected / exposed	22 / 39 (56.41%)	22 / 38 (57.89%)	
occurrences (all)	22	22	
Fever			
subjects affected / exposed	5 / 39 (12.82%)	9 / 38 (23.68%)	
occurrences (all)	5	9	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Cough			

subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Epistaxis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Investigations			
Fibrinogen increase			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
TCA increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Prothrombin time abnormal			
subjects affected / exposed	8 / 39 (20.51%)	10 / 38 (26.32%)	
occurrences (all)	8	10	
CPK Increased			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Hypoalbuminaemia			
subjects affected / exposed	10 / 39 (25.64%)	8 / 38 (21.05%)	
occurrences (all)	10	8	
Hyponatraemia			
subjects affected / exposed	3 / 39 (7.69%)	4 / 38 (10.53%)	
occurrences (all)	3	4	
Lipase			
subjects affected / exposed	0 / 39 (0.00%)	3 / 38 (7.89%)	
occurrences (all)	0	3	
Nervous system disorders			
Neuropathy sensitive			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			

Lymphopenia			
subjects affected / exposed	5 / 39 (12.82%)	6 / 38 (15.79%)	
occurrences (all)	5	6	
Leucocytosis			
subjects affected / exposed	31 / 39 (79.49%)	15 / 38 (39.47%)	
occurrences (all)	31	15	
Neutropenia			
subjects affected / exposed	33 / 39 (84.62%)	13 / 38 (34.21%)	
occurrences (all)	33	13	
Platelets decreased			
subjects affected / exposed	32 / 39 (82.05%)	27 / 38 (71.05%)	
occurrences (all)	32	27	
Anemia			
subjects affected / exposed	30 / 39 (76.92%)	27 / 38 (71.05%)	
occurrences (all)	30	27	
Gastrointestinal disorders			
Stomach pain			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Mucitis			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Abdominal pain			
subjects affected / exposed	18 / 39 (46.15%)	19 / 38 (50.00%)	
occurrences (all)	18	19	
Liver pain			
subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Anorexia			
subjects affected / exposed	12 / 39 (30.77%)	7 / 38 (18.42%)	
occurrences (all)	12	7	
Ascites			
subjects affected / exposed	3 / 39 (7.69%)	1 / 38 (2.63%)	
occurrences (all)	3	1	
Constipation			

subjects affected / exposed	3 / 39 (7.69%)	1 / 38 (2.63%)	
occurrences (all)	3	1	
Diarrhoea			
subjects affected / exposed	13 / 39 (33.33%)	6 / 38 (15.79%)	
occurrences (all)	13	6	
Dysgueusia			
subjects affected / exposed	3 / 39 (7.69%)	1 / 38 (2.63%)	
occurrences (all)	3	1	
Oral mucositis			
subjects affected / exposed	8 / 39 (20.51%)	0 / 38 (0.00%)	
occurrences (all)	8	0	
Nausea			
subjects affected / exposed	15 / 39 (38.46%)	4 / 38 (10.53%)	
occurrences (all)	15	4	
RGO			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Buccal dry			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	11 / 39 (28.21%)	5 / 38 (13.16%)	
occurrences (all)	11	5	
Hepatobiliary disorders			
Icter			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Alanine aminotransferase abnormal			
subjects affected / exposed	31 / 39 (79.49%)	29 / 38 (76.32%)	
occurrences (all)	31	29	
Aspartate aminotransferase abnormal			
subjects affected / exposed	37 / 39 (94.87%)	35 / 38 (92.11%)	
occurrences (all)	37	35	
Gamma-glutamyltransferase increased			

subjects affected / exposed	18 / 39 (46.15%)	15 / 38 (39.47%)	
occurrences (all)	18	15	
Bilirubin abnormal			
subjects affected / exposed	29 / 39 (74.36%)	27 / 38 (71.05%)	
occurrences (all)	29	27	
Liver failure			
subjects affected / exposed	4 / 39 (10.26%)	3 / 38 (7.89%)	
occurrences (all)	4	3	
Phophatases Alcalines abnormal			
subjects affected / exposed	31 / 39 (79.49%)	29 / 38 (76.32%)	
occurrences (all)	31	29	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Acneiform rash			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Dry skin			
subjects affected / exposed	6 / 39 (15.38%)	2 / 38 (5.26%)	
occurrences (all)	6	2	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	10 / 39 (25.64%)	3 / 38 (7.89%)	
occurrences (all)	10	3	
Renal and urinary disorders			
Creatinine renal clearance abnormal			
subjects affected / exposed	5 / 39 (12.82%)	10 / 38 (26.32%)	
occurrences (all)	5	10	
Acute renal failure			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Endocrine disorders			

Hyperthyroidism			
subjects affected / exposed	3 / 39 (7.69%)	1 / 38 (2.63%)	
occurrences (all)	3	1	
Hypothyroidism			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Hyperkaliemia			
subjects affected / exposed	1 / 39 (2.56%)	5 / 38 (13.16%)	
occurrences (all)	1	5	
Hypokaliemia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Weight loss			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	

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/32576496