Clinical trial results:
Nintedanib as maintenance treatment of malignant pleural mesothelioma (NEMO): a double-blind randomized phase II study of the EORTC Lung Cancer Group

Summary

EudraCT number	2016-000521-38
Trial protocol	BE GB IT
Global end of trial date	12 October 2023

Results information

Result version number	v1 (current)
This version publication date	14 September 2024
First version publication date	14 September 2024

Trial information

Trial identification

Sponsor protocol code	EORTC-08112

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02863055
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	EORTC
Sponsor organisation address	Avenue Emmanuel Mounier 83/11, Brussels, Belgium, 1200
Public contact	Regulatory Affairs Department, European Organisation for the Research and Treatment of Cancer, 0032 27741511, regulatory@eortc.org
Scientific contact	Regulatory Affairs Department, European Organisation for the Research and Treatment of Cancer, 0032 27741511, regulatory@eortc.org

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	30 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2023
Global end of trial reached?	Yes
Global end of trial date	12 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

the primary objective is to evaluate activity in terms of progression-free survival of nintedanib versus placebo as switch maintenance after first line chemotherapy treatment for patients with unresectable Malignant Pleural Mesothelioma

Protection of trial subjects:

Safety data were reviewed within EORTC Headquarters on a regular basis as part of the Medical Review process. Safety information was included in trial status reports which served as a basis of discussion during EORTC Group meetings.

Background therapy:

Before randomization, patients completed first-line platinum-based chemotherapy (4-6 weeks) for malignant pleural mesothelioma.

Evidence for comparator:

Placebo was used as a comparator. The role of maintenance pemetrexed after completion of 4-6 cycles of the platinum-based doublet chemotherapy was uncertain at the time of the study.

Actual start date of recruitment	15 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	37
EEA total number of subjects	11

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)	7
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study intended to randomize 114 patients. It was expected that 114 patients would be required to reach the required number of events within 28months (2.3 years) under a full accrual rate of 5 patients per month.
In total, 37 patients had been randomized by February 2021. Due to the poor accrual, the recruitment was terminated at that time.

Pre-assignment

Screening details:

Main eligibility criteria:

Age ≥18 years
ECOG performance status 0-2
histological diagnosis of unresectable Malignant Pleural Mesothelioma
Response or Stable disease according to modified RECIST criteria after first line platinum-pemetrexed chemotherapy for 4-6 cycles
adequate bone marrow, liver and renal function

Period 1

Period 1 title	Switch maintenance treament and placebo (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Subject, Assessor

Blinding implementation details:

This is a triple blind study. The patient, the investigator and study team at site and the EORTC Headquarters study team will remain blinded to treatment allocation up to the database lock for the final analysis of the primary endpoint.
However, at any time during the trial, in case of a safety concern affecting an individual patient, the site investigator can request the unblinding of that patient.

Arms

Are arms mutually exclusive?	Yes
Arm title	Nintedanib

Arm description:

Nintedanib 200 mg twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.

Arm type	Experimental
Investigational medicinal product name	Nintedanib
Investigational medicinal product code	BIBF 1120
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

400 mg (200 mg twice daily), continuous daily dosing until progression of disease or until criteria for interruption of treatment are met .

Dose reductions as needed were used in order to manage undue toxicities. Dose reduction steps: 200 mg twice daily - 150 mg twice daily - 100 mg twice daily - Stop protocol treatment.

If the dose of nintedanib had to be reduced due to adverse events it will stay on the lower dose level for the entire time of administration, reescalation is not allowed

Arm title	Placebo

Arm description:
Matching placebo twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.

Arm type	placebo

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Nintedanib	Placebo
Started	18	19
Completed	0	2
Not completed	18	17
Physician decision	1	-
Disease progression	14	16
Adverse event, non-fatal	2	-
COVID -19	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Nintedanib
Reporting group description:	
Nintedanib 200 mg twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.	

Reporting group title	Placebo
Reporting group description:	
Matching placebo twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.	

Reporting group values	Nintedanib	Placebo	Total
Number of subjects	18	19	37
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)	2	5	7
From 65-84 years	16	14	30
85 years and over	0	0	0
Age continuous Units: years			
median	71.5	69.0	
inter-quartile range (Q1-Q3)	67.0 to 77.0	64.0 to 72.0	-
Gender categorical Units: Subjects			
Female	6	4	10
Male	12	15	27
Baseline ECOG performance status			
Stratification factor used for randomization			
Units: Subjects			
ECOG - 0	6	8	14
ECOG - 1	12	11	23
Response to first line platinum-pemetrexed chemotherapy			
Stratification factor used for randomization			
Units: Subjects			
Partial Respone	5	5	10
Stable Disease	13	14	27
Complete Response	0	0	0
Histology type			
Stratification factor used for randomization			

Units: Subjects			
Epithelioid	14	15	29
Sarcomatoid	1	2	3
mixed/biphasic	3	2	5
Height			
Units: cm			
median	170.0	172.5	
inter-quartile range (Q1-Q3)	158.0 to 176.0	164.0 to 176.0	-
Body weight			
Units: cm			
median	76.8	78.1	
inter-quartile range (Q1-Q3)	65.2 to 84.0	67.6 to 82.4	-

Subject analysis sets

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

All patients who are eligible and have started their allocated treatment (at least one dose of the study drug(s) in chemotherapy trials)

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who have started their allocated treatment (at least one dose of the study drug(s) in chemotherapy trials)

Reporting group values	Per Protocol	Safety	
Number of subjects	36	37	
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)	6	7	
From 65-84 years	30	30	
85 years and over	0	0	
Age continuous			
Units: years			
median			
inter-quartile range (Q1-Q3)			
Gender categorical			
Units: Subjects			
Female			
Male			
Baseline ECOG performance status			
Stratification factor used for randomization			
Units: Subjects			

ECOG - 0 ECOG - 1			
Response to first line platinum-pemetrexed chemotherapy			
Stratification factor used for randomization			
Units: Subjects			
Partial Respone Stable Disease Complete Response			
Histology type			
Stratification factor used for randomization			
Units: Subjects			
Epithelioid Sarcomatoid mixed/biphasic			
Height Units: cm median inter-quartile range (Q1-Q3)			
Body weight Units: cm median inter-quartile range (Q1-Q3)			

End points

End points reporting groups

Reporting group title	Nintedanib

Reporting group description:

Nintedanib 200 mg twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.

Reporting group title	Placebo

Reporting group description:

Matching placebo twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

All patients who are eligible and have started their allocated treatment (at least one dose of the study drug(s) in chemotherapy trials)

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who have started their allocated treatment (at least one dose of the study drug(s) in chemotherapy trials)

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

Progression Free Survival (PFS) is defined as the time interval between the date of randomization and the
date of disease progression, recurrence or death, whichever comes first. If neither event has been observed, then the patient is censored at the date of the last follow up examination

End point type	Primary

End point timeframe:

Originally planned after reaching 95 PFS events. The accrual was stopped prematurely due to the low accrual rate February 5th 2021 . The analysis was performed on the 37 eligible at the clinical cut-off date of the 30th of April 2023.

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Months				
median (confidence interval 70%)	3.43 (3.32 to 5.55)	4.58 (3.65 to 9.00)		

Statistical analyses

Statistical analysis title	Primary: Progression-free survival

Statistical analysis description:

Due to poor accrual, and recruiting only 37 patients (36 in the per-protocol analysis set) rather than the planned 114 patients, the statistical analysis of this (primary) endpoint is only descriptive.
The analysis is performed on the per-protocol population. HR values smaller than 1 indicate longer PFS in the experimental arm.
HR values larger than 1 indicate shorter PFS in the experimental arm.

Comparison groups	Nintedanib v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.25
Confidence interval	
level	Other: 70 %
sides	2-sided
lower limit	1.52
upper limit	3.32

Secondary: Overall response rate

End point title	Overall response rate

End point description:

The overall response rate is defined as an overall rate including patients with documented complete response (CR) or partial response (PR) where CR and PR are defined according to the RECIST criteria. The baseline for this assessment is set after the induction chemotherapy and within 3 weeks prior to randomization.

End point type	Secondary

End point timeframe:

Between the 24th April 2018 and the 3rd of February 2021

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Events				
Complete Response	0	0		
Partial Response	0	1		
Stable Disease	10	13		
Progressive Disease	8	3		
Missing	0	1		

Statistical analyses

Statistical analysis title	Overall Response Rate experimental arm

Statistical analysis description:

The overall response rate is defined as an overall rate including patients with documented complete response or partial response. Stable disease, progressive disease, early death and unknown(missing)

response status are considered as failures to respond to treatment.

Comparison groups	Placebo v Nintedanib
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Response Rate %
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	Overall Response Rate placebo arm

Statistical analysis description:

The overall response rate is defined as an overall rate including patients with documented complete response or partial response. Stable disease, progressive disease, early death and unknown(missing) response status are considered as failures to respond to treatment.

Comparison groups	Placebo v Nintedanib
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Response Rate %
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	27.3

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival time is computed from date of registration until date of death from any cause. If no death has been observed, then the patient is censored at the last date known to be alive. The analysis is performed on the per-protocol population
The value 99999 is used when the upper limit of a confidence interval has not been reached

End point type	Secondary

End point timeframe:

xxx

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Months				
median (confidence interval 70%)	13.13 (11.17 to 18.56)	38.93 (27.66 to 99999)		

Statistical analyses

Statistical analysis title	Secondary: Overall Survival
Statistical analysis description:	
HR values larger than 1 indicate shorter Overall Survival in the experimental arm.	
Comparison groups	Nintedanib v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.27
Confidence interval	
level	Other: 70 %
sides	2-sided
lower limit	1.48
upper limit	3.49

Secondary: TIme to Treatment Failure

End point title	TIme to Treatment Failure
End point description:	
Time to treatment Failure (TTF) is defined as the time interval between the date of randomization and discontinuation for any reason, including disease progression, treatment toxicity, normal completion, patient preference, or death. If no event has been observed, then the patient is censored at the last date of disease evaluation.	
End point type	Secondary
End point timeframe:	
xxx	

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Months				
median (confidence interval 70%)	2.00 (1.87 to 4.24)	4.63 (3.71 to 8.31)		

Statistical analyses

Statistical analysis title	Secondary: Time to treatment failure
Statistical analysis description: HR values larger than 1 indicate shorter time-to-treatment failure in the experimental arm.	
Comparison groups	Nintedanib v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.56
Confidence interval	
level	Other: 70 %
sides	2-sided
lower limit	1.74
upper limit	3.78

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The number of patients who had specific adverse events in the period between the randomization and the time of treatment (including placebo treatment) discontinuation was reported. The maximum was ...

Adverse event reporting additional description:

Adverse events are evaluated using CTC grading. Serious adverse events were defined following the Good Clinical Practice Guideline.
Adverse events are reported as belonging to the treatment period if the adverse event start date falls on the first day of treatment and up till the
date of last treatment administration + 30 days.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Nintedanib

Reporting group description:

Nintedanib 200 mg twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.

Reporting group title	Placebo

Reporting group description:

Matching placebo twice daily until objective evidence of progression, uncontrollable toxicity, patient or physician decision (in case of symptomatic progression) or death.

Serious adverse events	Nintedanib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 18 (38.89%)	0 / 19 (0.00%)	
number of deaths (all causes)	15	10	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (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			

Malaise			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Nintedanib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	10 / 19 (52.63%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 18 (11.11%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	2 / 18 (11.11%)	3 / 19 (15.79%)	
occurrences (all)	2	3	
flu like symptoms			
subjects affected / exposed	0 / 18 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Malaise			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 18 (5.56%)	4 / 19 (21.05%)	
occurrences (all)	1	4	
Reproductive system and breast disorders			
Testicular disorder			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Bronchial obstruction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	5 / 18 (27.78%)	2 / 19 (10.53%)	
occurrences (all)	5	2	
Dyspnoea			
subjects affected / exposed	3 / 18 (16.67%)	3 / 19 (15.79%)	
occurrences (all)	3	3	
Pleural effusion			
subjects affected / exposed	2 / 18 (11.11%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Pleuritic pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Wheezing			

subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Other			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Investigations			
Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
creatinine increased			
subjects affected / exposed	0 / 18 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
GGT increased			
subjects affected / exposed	3 / 18 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
INR increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Lymphoblast count Decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Sinus bradycardia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	0 / 18 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	3 / 18 (16.67%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Neuralgia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
paresthesia			
subjects affected / exposed	3 / 18 (16.67%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Other			

subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 18 (27.78%)	1 / 19 (5.26%)	
occurrences (all)	5	1	
Constipation			
subjects affected / exposed	3 / 18 (16.67%)	2 / 19 (10.53%)	
occurrences (all)	3	2	
Diarrhoea			
subjects affected / exposed	10 / 18 (55.56%)	3 / 19 (15.79%)	
occurrences (all)	10	3	
Dysphagia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Gastroesophageal Reflux Disease			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Mucositis oral			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	10 / 18 (55.56%)	1 / 19 (5.26%)	
occurrences (all)	10	1	
Periodontal disease			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	6 / 18 (33.33%)	3 / 19 (15.79%)	
occurrences (all)	6	3	
Hepatobiliary disorders			
other			

subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Renal and urinary disorders			
hematuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Renal Calculi			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Urinary Frequency			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Bone pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
chest wall pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			

subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
bronchial infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
lung infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Upper respiratory infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
other			
subjects affected / exposed	0 / 18 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was closed prematurely due to poor accrual. The planned sample size was not reached for any of the endpoints. The performed analysis has a descriptive character.

Notes: