Clinical trial results:
A phase II study exploring the safety and efficacy of nintedanib (BIBF1120) as second line therapy for patients with either differentiated or medullary thyroid cancer progressing after first line therapy.

Summary

EudraCT number	2012-004295-19
Trial protocol	BE IT GB NL DK FR ES PL
Global end of trial date	28 August 2019

Results information

Result version number	v1 (current)
This version publication date	01 May 2020
First version publication date	01 May 2020

Trial information

Trial identification

Sponsor protocol code	1209

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01788982
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	European Organisation for the Research and Treatment of Cancer
Sponsor organisation address	Avenue E. Mounier 83/11 , Brussels, Belgium, 1200
Public contact	Regulatory Affairs Department, European Organisation for the Research and Treatment of Cancer, +32 2 774 1023, regulatory@eortc.be
Scientific contact	Regulatory Affairs Department, European Organisation for the Research and Treatment of Cancer, +32 2 774 1023, regulatory@eortc.be

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 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2019
Global end of trial reached?	Yes
Global end of trial date	28 August 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to explore the efficacy of nintedanib (as measured by progression free survival) as second line therapy for patients with either differentiated or medullary thyroid cancer progressing after first line therapy.

Protection of trial subjects:

Protection of trial subjects:
The responsible investigator ensured that this study was conducted in agreement with either the Declaration of Helsinki (available on the World Medical Association web site (http://www.wma.net)) and/or the laws and regulations of the country, whichever provides the greatest protection of the patient. The protocol had been written, and the study was conducted according to the ICH Harmonized Tripartite Guideline on Good Clinical Practice (ICH-GCP, available online at http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf). The protocol was approved by the competent ethics committee(s) as required by the applicable national legislation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 12
Worldwide total number of subjects	102
EEA total number of subjects	102

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)	57
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was screened on 18 June, 2014. On 21 February, 2018, when accrual to the study was closed for poor accrual, 102 patients were registered in the study by 22 sites in 9 countries.
Of the 102 patients who were screened and registered, 101 (99%) were randomized.

Pre-assignment

Screening details:

Histologically confirmed differentiated or medullary thyroid cancer by local pathologist; Locally advanced or metastatic disease deemed incurable by surgery, radiotherapy, RAI; must have received at least one but no more than two line(s) of treatment; Age ≥18 years; WHO performance status 0-1; Life expectancy > 12 weeks.

Period 1

Period 1 title	Blinded period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	DTC - Placebo

Arm description:

Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Placebo.

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

Dosage and administration details:

Dosage: Capsules matching 400 mg of Nintedanib (200 mg twice daily), contains 0 mg of Nintedanib.
Administration details: Two capsules of 100mg should be swallowed in the morning and two capsules of 100mg should be swallowed in the evening unchewed with a glass of water of about 250 ml. The dose interval should be around 12 hours at the same time every day, usually in the morning and the evening after food intake. Continues until progression of disease or until criteria for interruption of treatment are met.

Arm title	DTC - Nintedanib

Arm description:

Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Nintedanib.

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

Dosage and administration details:

Dosage: 400 mg (200 mg twice daily).
Administration details: Two capsules each containing 100mg nintedanib should be swallowed in the morning and two capsules each containing 100mg nintedanib should be swallowed in the evening unchewed with a glass of water of about 250 ml. The dose interval should be around 12 hours at the same time every day, usually in the morning and the evening after food intake. Daily dosing continues

until progression of disease or until criteria for interruption of treatment are met.

Arm title	MTC - Placebo

Arm description:

Patients diagnosed as Medullary Thyroid Cancer (MTC) who were randomized to receive Placebo.

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

Dosage and administration details:

Dosage: Capsules matching 400 mg of Nintedanib (200 mg twice daily), contains 0 mg of Nintedanib.
Administration details: Two capsules of 100mg should be swallowed in the morning and two capsules of 100mg should be swallowed in the evening unchewed with a glass of water of about 250 ml. The dose interval should be around 12 hours at the same time every day, usually in the morning and the evening after food intake. Continues until progression of disease or until criteria for interruption of treatment are met.

Arm title	MTC - Nintedanib

Arm description:

Patients diagnosed as Medullary Thyroid Cancer (MTC) who were randomized to receive Nintedanib.

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

Dosage and administration details:

Dosage: 400 mg (200 mg twice daily).
Administration details: Two capsules each containing 100mg nintedanib should be swallowed in the morning and two capsules each containing 100mg nintedanib should be swallowed in the evening unchewed with a glass of water of about 250 ml. The dose interval should be around 12 hours at the same time every day, usually in the morning and the evening after food intake. Daily dosing continues until progression of disease or until criteria for interruption of treatment are met.

Number of subjects in period 1[1]	DTC - Placebo	DTC - Nintedanib	MTC - Placebo
Started	25	45	9
Completed	25	44	9
Not completed	0	1	0
Early death prior to planned start of treatment	-	1	-

Number of subjects in period 1[1]	MTC - Nintedanib
Started	22

Completed	22
Not completed	0
Early death prior to planned start of treatment	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Only patients that were randomized are reported in the baseline period. As one patient was enrolled but not randomized due to fast general deterioration, only 101/102 patients were reported for the baseline period.

Period 2

Period 2 title	Open-label period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Cross-over

Arm description:

Patients in placebo arm who chose to cross over to receive Nintedanib upon progression.

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

Dosage and administration details:

Dosage: 400 mg (200 mg twice daily).
Administration details: Two capsules each containing 100mg nintedanib should be swallowed in the morning and two capsules each containing 100mg nintedanib should be swallowed in the evening unchewed with a glass of water of about 250 ml. The dose interval should be around 12 hours at the same time every day, usually in the morning and the evening after food intake. Daily dosing continues until progression of disease or until criteria for interruption of treatment are met.

Number of subjects in period 2[2]	Cross-over
Started	22
Completed	21
Not completed	1
Lost to follow-up	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The second period only consists of patients from the blinded period that progressed under placebo and chose to cross-over to the experimental treatment (Nintedanib). As such it only corresponds to a small number of patients from the preceding period, not all of them.

Baseline characteristics

Reporting groups	
Reporting group title	DTC - Placebo
Reporting group description:	
Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Placebo.	
Reporting group title	DTC - Nintedanib
Reporting group description:	
Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Nintedanib.	
Reporting group title	MTC - Placebo
Reporting group description:	
Patients diagnosed as Medullary Thyroid Cancer (MTC) who were randomized to receive Placebo.	
Reporting group title	MTC - Nintedanib
Reporting group description:	
Patients diagnosed as Medullary Thyroid Cancer (MTC) who were randomized to receive Nintedanib.	

Reporting group values	DTC - Placebo	DTC - Nintedanib	MTC - Placebo
Number of subjects	25	45	9
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)	13	20	7
From 65-84 years	12	25	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	14	25	2
Male	11	20	7

Reporting group values	MTC - Nintedanib	Total	
Number of subjects	22	101	
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)	16	56	
From 65-84 years	6	45	

85 years and over	0	0	

Gender categorical Units: Subjects			
Female	6	47	
Male	16	54	

End points

End points reporting groups

Reporting group title	DTC - Placebo
Reporting group description:	
Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Placebo.	
Reporting group title	DTC - Nintedanib
Reporting group description:	
Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Nintedanib.	
Reporting group title	MTC - Placebo
Reporting group description:	
Patients diagnosed as Medullary Thyroid Cancer (MTC) who were randomized to receive Placebo.	
Reporting group title	MTC - Nintedanib
Reporting group description:	
Patients diagnosed as Medullary Thyroid Cancer (MTC) who were randomized to receive Nintedanib.	
Reporting group title	Cross-over
Reporting group description:	
Patients in placebo arm who chose to cross over to receive Nintedanib upon progression.	

Primary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
End point description:	
All survival estimates and statistical analyses reported for that endpoint are done on the Per Protocol (PP) population: all eligible patients that started their randomized treatment.	
End point type	Primary
End point timeframe:	
Progression Free Survival (PFS) is defined as the time interval between the date of randomization and the date of disease progression or death, whichever comes first.	

End point values	DTC - Placebo	DTC - Nintedanib	MTC - Placebo	MTC - Nintedanib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	37	5	15
Units: % at 5 months				
number (confidence interval 80%)	36.8 (23.0 to 50.7)	46.0 (35.2 to 56.0)	40.0 (13.9 to 65.3)	60.0 (42.0 to 74.0)

Statistical analyses

Statistical analysis title	Primary analysis - DTC
Statistical analysis description:	
The comparison for the primary endpoint was performed on the Per Protocol population. Cox regression was used to compare the experimental versus the control arms in DTC patients, stratified by country, with 1-sided 10% significant level test.	
Comparison groups	DTC - Placebo v DTC - Nintedanib

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0947
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.65
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.42
upper limit	0.99

Statistical analysis title	Primary analysis - MTC

Statistical analysis description:

This analysis was done on the Per Protocol population. Since the study did not reach the targeted statistical power, no inferential test were performed for the MTC cohort. Only the unadjusted treatment effect (univariate, no stratification factors) from Cox model were reported with its 95% confidence interval, as defined in the modified Statistical Analysis Plan (SAP).

Comparison groups	MTC - Placebo v MTC - Nintedanib
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.53

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

All survival estimates and statistical analyses reported for that endpoint are done on the Per Protocol (PP) population: all eligible patients that started their randomized treatment.

End point type	Secondary

End point timeframe:

Overall Survival (OS) is defined as the time interval between the date of randomization and the date of death from any cause. If no event has been observed, then the patient is censored at the last date known to be alive.

End point values	DTC - Placebo	DTC - Nintedanib	MTC - Placebo	MTC - Nintedanib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	37	5	15
Units: % at 5 months				
number (confidence interval 80%)	84.2 (69.7 to 92.1)	89.0 (80.1 to 94.0)	999 (999 to 999)	93.3 (78.0 to 98.1)

Statistical analyses

Statistical analysis title	Primary analysis - DTC

Statistical analysis description:

This analysis is applied on the Per Protocol population, with the secondary endpoint of Overall Survival this time. Cox regression was used to compare the experimental versus the control arms in DTC patients, stratified by country, with 1-sided 10% significant level test.

Comparison groups	DTC - Placebo v DTC - Nintedanib
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4969
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	Other: 0.8 %
sides	2-sided
lower limit	0.54
upper limit	1.84

Statistical analysis title	Primary analysis - MTC

Statistical analysis description:

This analysis was done on the Per Protocol population, for overall survival this time. Since the study did not reach the targeted statistical power, no inferential test were performed for the MTC cohort. Only the unadjusted treatment effect (univariate, no stratification factors) from Cox model were reported with its 95% confidence interval, in accordance with the modified Statistical Analysis Plan (SAP).

Comparison groups	MTC - Placebo v MTC - Nintedanib
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	3.21

Secondary: PFS at second progression (PFS-2)

End point title	PFS at second progression (PFS-2)

End point description:

The results are reported for the Per Protocol (PP) population. All eligible patients that started their randomized treatment (during the blinded period).

End point type	Secondary

End point timeframe:

This endpoint is only applicable for patients in placebo arm who cross over to receive Nintedanib upon first progression. PFS-2 is calculated as the time between randomization and second progression or death, whichever comes first.

End point values	Cross-over			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: % at 5 months				
number (confidence interval 80%)	87.5 (71.8 to 94.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected on a CRF to be submitted at pre-specified timepoint:
-During treatment, on first day of each cycle prior treatment administration
-At the end of protocol visit (4 weeks (+/- 1 week) after last treatment administration)

Adverse event reporting additional description:

Reporting of AEs and SAE are limited to the blinded (randomized) period and is done according to NCI-CTCAE v 4.0.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	DTC - Placebo

Reporting group description:

Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Placebo.

Reporting group title	DTC - Nintedanib

Reporting group description:

Patients diagnosed as Differentiated Thyroid Cancer (DTC) who were randomized to receive Nintedanib.

Reporting group title	MTC - Placebo

Reporting group description:

Patients diagnosed as Medullary Thyroid Cancer (DTC) who were randomized to receive Placebo.

Reporting group title	MTC - Nintedanib

Reporting group description:

Patients diagnosed as Medullary Thyroid Cancer (DTC) who were randomized to receive Nintedanib.

Serious adverse events	DTC - Placebo	DTC - Nintedanib	MTC - Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 25 (28.00%)	10 / 44 (22.73%)	5 / 9 (55.56%)
number of deaths (all causes)	18	30	6
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
NEOPLASM PROGRESSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
SUPERIOR VENA CAVA SYNDROME			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENA CAVA THROMBOSIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
DEATH			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
INFLUENZA LIKE ILLNESS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
LUNG DISORDER			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
RESPIRATORY FAILURE			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DEPRESSED MOOD			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIVER FUNCTION TEST ABNORMAL			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIAC FAILURE ACUTE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CEREBRAL INFARCTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
CEREBROVASCULAR ACCIDENT			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
HEADACHE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCIATICA			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
COLONIC FISTULA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULAR PERFORATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC FUNCTION ABNORMAL			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTRANSAMINASAEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
DEVICE RELATED INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPPORTUNISTIC INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERCALCAEMIA			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOCALCAEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MTC - Nintedanib		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 22 (31.82%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
NEOPLASM PROGRESSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
SUPERIOR VENA CAVA SYNDROME			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VENA CAVA THROMBOSIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
DEATH			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFLUENZA LIKE ILLNESS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
LUNG DISORDER				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY FAILURE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
DEPRESSED MOOD				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
ALANINE AMINOTRANSFERASE INCREASED				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ASPARTATE AMINOTRANSFERASE INCREASED				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LIVER FUNCTION TEST ABNORMAL				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
ATRIAL FIBRILLATION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
CARDIAC ARREST				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CARDIAC FAILURE ACUTE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PERICARDIAL EFFUSION				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
CEREBRAL INFARCTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CEREBROVASCULAR ACCIDENT			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEADACHE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SCIATICA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
ANAEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
COLONIC FISTULA			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIVERTICULAR PERFORATION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VOMITING				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
CHOLECYSTITIS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HEPATIC FUNCTION ABNORMAL				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPERTRANSAMINASAEMIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
ACUTE KIDNEY INJURY				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
DEVICE RELATED INFECTION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ERYSIPELAS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OPPORTUNISTIC INFECTION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
SEPSIS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
DECREASED APPETITE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPERCALCAEMIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPOCALCAEMIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	DTC - Placebo	DTC - Nintedanib	MTC - Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 25 (100.00%)	41 / 44 (93.18%)	8 / 9 (88.89%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOR PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	3	4	0
Vascular disorders			
FLUSHING			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	6 / 25 (24.00%)	13 / 44 (29.55%)	2 / 9 (22.22%)
occurrences (all)	12	23	5
THROMBOEMBOLIC EVENT			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	2 / 44 (4.55%)	1 / 9 (11.11%)
occurrences (all)	2	6	1
WHITE FINGERS IN THE COLD			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
AMPUTATION TOE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
EDEMA LIMBS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

FATIGUE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	7 / 25 (28.00%)	15 / 44 (34.09%)	5 / 9 (55.56%)
occurrences (all)	8	26	5
FEVER			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	3 / 44 (6.82%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
FLU LIKE SYMPTOMS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GAIT DISTURBANCE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LOCALIZED EDEMA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
MALAISE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	3 / 44 (6.82%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
THORACIC PAIN			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
ALLERGIC REACTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
ALLERGIC REACTION TO BLOOD TRANSFUSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
ALLERGIC RHINITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BRONCHOPULMONARY HEMORRHAGE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
COUGH			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	3 / 44 (6.82%)	0 / 9 (0.00%)
occurrences (all)	0	8	0
DYSPNEA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	6 / 25 (24.00%)	8 / 44 (18.18%)	1 / 9 (11.11%)
occurrences (all)	9	10	1
PHARYNGEAL MUCOSITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PLEURAL EFFUSION			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PNEUMONIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PNEUMONITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
RESPIRATORY INSUFFISIENCY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
AGITATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
ANXIETY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
DEPRESSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
INSOMNIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALKALINE PHOSPHATASE INCREASED			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
C REACTIVE PROTEIN INCREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
C REACTIVE PROTEINE INCREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GGT INCREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	4 / 44 (9.09%)	0 / 9 (0.00%)
occurrences (all)	2	5	0
IRON INSUFFICIENCY alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LYMPHOCYTE COUNT DECREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SERUM AMYLASE INCREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VITAMIN B9 DEFICIENCY alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
WEIGHT GAIN alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0

WEIGHT LOSS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	6 / 25 (24.00%)	10 / 44 (22.73%)	3 / 9 (33.33%)
occurrences (all)	8	15	5
Injury, poisoning and procedural complications			
FOOD POISONING			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cardiac disorders			
ATRIAL FIBRILLATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	4	1	0
CARDIAC ARREST			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HEART FAILURE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PALPITATIONS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
PERICARDIAL EFFUSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DEPRESSED LEVEL OF CONSCIOUSNESS			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
DIZZINESS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
DYSGEUSIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
FACIAL PARESIS LEFT			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HEADACHE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	5 / 44 (11.36%)	1 / 9 (11.11%)
occurrences (all)	1	10	1
INSIPIENT MECHANICAL CORD COMPRESSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
INTRACRANIAL HEMORRHAGE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
LETHARGY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LINGUAL PARESTHESIAS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

PARAPLEGIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PARESTHESIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL MOTOR NEUROPATHY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RADICULITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SOMNOLENCE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SPINAL CORD COMPRESSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
STROKE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

NEUTROPHILIC LEUKOCYTOSIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
BLURRED VISION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
LOSS OF VISION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	7 / 44 (15.91%)	0 / 9 (0.00%)
occurrences (all)	1	10	0
ANAL HEMORRHAGE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
COLITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
COLONIC PERFORATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CONSTIPATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	3 / 44 (6.82%)	0 / 9 (0.00%)
occurrences (all)	0	5	0
DIARRHEA			

alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	22 / 44 (50.00%)	4 / 9 (44.44%)
occurrences (all)	3	37	4
DRY MOUTH			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
DYSPHAGIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ENTEROCOLITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GASTRITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GASTROESOPHAGEAL REFLUX DISEASE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
GASTROINTESTINAL PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INTERMITANT INDEGESTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LOSS OF APETITE			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MUCOSITIS ORAL alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
NAUSEA alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	15 / 44 (34.09%)	1 / 9 (11.11%)
occurrences (all)	2	22	1
ORAL PAIN alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
STOMACH PAIN alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	4 / 44 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	7	0
VOMITING alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	3 / 25 (12.00%)	11 / 44 (25.00%)	0 / 9 (0.00%)
occurrences (all)	3	16	0
Hepatobiliary disorders CHOLECYSTITIS alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders ALOPECIA alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	4 / 44 (9.09%)	0 / 9 (0.00%)
occurrences (all)	2	4	0
BLEEDING FROM THE NECK TUMOR (SKIN INFILTRATION) alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DRY SKIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	4 / 25 (16.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	4	0	1
ERYTHEMA RIGHT UPPER LEG			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LEFT THORACIC CUTANEOUS PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PAIN OF SKIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PALMAR-PLANTAR ERYTHRODYSESTHESIA SYNDROME			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
PRURITUS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
RASH (SHAVING)			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RASH ACNEIFORM			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

RASH MACULO-PAPULAR			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	2 / 44 (4.55%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
SCALP DISCOLORATIONS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SKIN INDURATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
URTICARIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HEMATURIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RENAL COLIC			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
URINARY RETENTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			

HYPERTHYROIDISM			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
ARTHRITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BACK PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
BONE PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
CHEST WALL PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
CRAMPING LEFT FOOT			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
FLANK PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
LUMBOISCHIALGIA			
alternative dictionary used: NCI-			

CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
MUSCLE PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
MYALGIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	3 / 25 (12.00%)	3 / 44 (6.82%)	0 / 9 (0.00%)
occurrences (all)	3	4	0
NECK PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
NIGHT CRAMPS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
NIGHT LOWER LIMBS CRAMPS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
SCAPULA PAIN			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
ARTERITIS INFECTIVE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BRONCHIAL INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 25 (8.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
LUNG INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
OPPORTUNISTIC INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SEPSIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SINUSITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SYSTEMIC NOT CONTROLLED INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
TRACHEITIS			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	1 / 25 (4.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
UPPER RESPIRATORY INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	2 / 44 (4.55%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
URINARY TRACT INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
WOUND INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
ANOREXIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	3 / 25 (12.00%)	12 / 44 (27.27%)	3 / 9 (33.33%)
occurrences (all)	3	18	3
DEHYDRATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HYPERALBUMINEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERCALCEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCEMIA			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	2 / 25 (8.00%)	0 / 44 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
HYPOCALCEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 25 (4.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
HYPOKALEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
HYPONATREMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 25 (0.00%)	1 / 44 (2.27%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	MTC - Nintedanib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOR PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Vascular disorders			
FLUSHING			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
HYPERTENSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	13		
THROMBOEMBOLIC EVENT			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
WHITE FINGERS IN THE COLD			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Surgical and medical procedures			
AMPUTATION TOE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
General disorders and administration site conditions			
EDEMA LIMBS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
FATIGUE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	8 / 22 (36.36%)		
occurrences (all)	15		
FEVER			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
FLU LIKE SYMPTOMS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
GAIT DISTURBANCE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
LOCALIZED EDEMA			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
MALAISE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
NON-CARDIAC CHEST PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
THORACIC PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Immune system disorders			
ALLERGIC REACTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
ALLERGIC REACTION TO BLOOD TRANSFUSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
ALLERGIC RHINITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
BRONCHOPULMONARY HEMORRHAGE			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
COUGH			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
DYSPNEA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
PHARYNGEAL MUCOSITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
PLEURAL EFFUSION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
PNEUMONIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
PNEUMONITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
RESPIRATORY INSUFFISIENCY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
AGITATION			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
ANXIETY				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
DEPRESSION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
INSOMNIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Investigations				
ALKALINE PHOSPHATASE INCREASED				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
C REACTIVE PROTEIN INCREASED				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
C REACTIVE PROTEINE INCREASED				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
GGT INCREASED				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	4 / 22 (18.18%)			
occurrences (all)	7			
IRON INSUFFICIENCY				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
LYMPHOCYTE COUNT DECREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
SERUM AMYLASE INCREASED alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
VITAMIN B9 DEFICIENCY alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
WEIGHT GAIN alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
WEIGHT LOSS alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	9 / 22 (40.91%)		
occurrences (all)	13		
Injury, poisoning and procedural complications			
FOOD POISONING alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
ATRIAL FIBRILLATION alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
CARDIAC ARREST alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
HEART FAILURE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
PALPITATIONS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
PERICARDIAL EFFUSION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	2			
Nervous system disorders				
DEPRESSED LEVEL OF CONSCIOUSNESS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
DIZZINESS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
DYSGEUSIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
FACIAL PARESIS LEFT				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
HEADACHE				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	2			
INSIPIENT MECHANICAL CORD COMPRESSION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
INTRACRANIAL HEMORRHAGE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
LETHARGY				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	4 / 22 (18.18%)			
occurrences (all)	5			
LINGUAL PARESTHESIAS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
PARAPLEGIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
PARESTHESIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	2			
PERIPHERAL MOTOR NEUROPATHY				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
RADICULITIS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			

SCIATICA alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) SOMNOLENCE alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) SPINAL CORD COMPRESSION alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) STROKE alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0		
Blood and lymphatic system disorders NEUTROPHILIC LEUKOCYTOSIS alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Eye disorders BLURRED VISION alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) LOSS OF VISION alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0 0 / 22 (0.00%) 0		
Gastrointestinal disorders ABDOMINAL PAIN alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) ANAL HEMORRHAGE	3 / 22 (13.64%) 3		

alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
COLITIS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
COLONIC PERFORATION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
CONSTIPATION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences (all)	4			
DIARRHEA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	12 / 22 (54.55%)			
occurrences (all)	26			
DRY MOUTH				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
DYSPHAGIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
ENTEROCOLITIS				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
GASTRITIS				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
GASTROESOPHAGEAL REFLUX DISEASE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
GASTROINTESTINAL PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
INTERMITANT INDEGESTION				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
LOSS OF APETITE				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
MUCOSITIS ORAL				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
NAUSEA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	8 / 22 (36.36%)			
occurrences (all)	14			
ORAL PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
STOMACH PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			

VOMITING			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Hepatobiliary disorders			
CHOLECYSTITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
ALOPECIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
BLEEDING FROM THE NECK TUMOR (SKIN INFILTRATION)			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
DRY SKIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
ERYTHEMA RIGHT UPPER LEG			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
LEFT THORACIC CUTANEOUS PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
PAIN OF SKIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
PALMAR-PLANTAR			

ERYTHRODYSESTHESIA SYNDROME			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
PRURITUS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
RASH (SHAVING)			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
RASH ACNEIFORM			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
RASH MACULO-PAPULAR			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
SCALP DISCOLORATIONS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
SKIN INDURATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
URTICARIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

ACUTE KIDNEY INJURY alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) HEMATURIA alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) RENAL COLIC alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) URINARY RETENTION alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0 1 / 22 (4.55%) 1 1 / 22 (4.55%) 3 0 / 22 (0.00%) 0			
Endocrine disorders HYPERTHYROIDISM alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0			
Musculoskeletal and connective tissue disorders ARTHRALGIA alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) ARTHRITIS alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) BACK PAIN alternative dictionary used: NCI-CTCAE 4.0 subjects affected / exposed occurrences (all) BONE PAIN	0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 1 / 22 (4.55%) 1			

alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
CHEST WALL PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
CRAMPING LEFT FOOT				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
FLANK PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
LUMBOISCHIALGIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
MUSCLE PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
MYALGIA				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
NECK PAIN				
alternative dictionary used: NCI-CTCAE 4.0				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
NIGHT CRAMPS				
alternative dictionary used: NCI-CTCAE 4.0				

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
NIGHT LOWER LIMBS CRAMPS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
PAIN IN EXTREMITY			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
SCAPULA PAIN			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Infections and infestations			
ARTERITIS INFECTIVE			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
BRONCHIAL INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
LUNG INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
OPPORTUNISTIC INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
SEPSIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
SINUSITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
SYSTEMIC NOT CONTROLLED INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
TRACHEITIS			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
UPPER RESPIRATORY INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
URINARY TRACT INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
WOUND INFECTION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
ANOREXIA			
alternative dictionary used: NCI-CTCAE 4.0			

subjects affected / exposed	9 / 22 (40.91%)		
occurrences (all)	14		
DEHYDRATION			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
HYPERALBUMINEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
HYPERCALCEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
HYPERGLYCEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
HYPOCALCEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
HYPOKALEMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
HYPONATREMIA			
alternative dictionary used: NCI-CTCAE 4.0			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		

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.

Since the study did not reach the targeted statistical power for the final analysis of MTC cohort, no inferential tests were performed.

Notes: