



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
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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
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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
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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	
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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
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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)
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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
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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)
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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
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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
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Dictionary used

Dictionary name	NCI-CTCAE
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Dictionary version	4.0
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Reporting groups

Reporting group title	DTC - Placebo
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Reporting group description:

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

Reporting group title	DTC - Nintedanib
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Reporting group description:

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

Reporting group title	MTC - Placebo
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Reporting group description:

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

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

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

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

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

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

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

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

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			

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

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

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 INSUFFICIENCY			
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			

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

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

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

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		

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

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

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			

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

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: