Clinical trial results:
A Phase II, Open-label, Study in Subjects with BRAF V600E-Mutated Rare Cancers with Several Histologies to Investigate the Clinical Efficacy and Safety of the Combination Therapy of Dabrafenib and Trametinib

Summary

EudraCT number	2013-001705-87
Trial protocol	IT SE BE AT DK NL ES NO
Global end of trial date	10 December 2021

Results information

Result version number	v2 (current)
This version publication date	15 September 2023
First version publication date	16 December 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	117019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02034110
WHO universal trial number (UTN)	-
Other trial identifiers	Novartis: CDRB436X2201, GlaxoSmithKline: BRF117019

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

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	10 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2021
Global end of trial reached?	Yes
Global end of trial date	10 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine Overall Response Rate (ORR) of dabrafenib + trametinib in subjects with selected rare BRAF V600E-mutated cancers.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United States: 91
Worldwide total number of subjects	206
EEA total number of subjects	91

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)	122
From 65 to 84 years	81
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 41 centers in 14 countries worldwide.

Pre-assignment

Screening details:

Subjects were enrolled into cohorts based on the type of histology. For each histology, up to 25 patients were planned to be enrolled. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Anaplastic Thyroid Cancer (ATC)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	Biliary Tract Cancer (BTC)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	Gastrointestinal Stromal Tumor (GIST)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	Low Grade (WHO G1/G2) Glioma (LGG)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	High Grade (WHO G3/G4) Glioma (HGG)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental

Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	Adenocarcinoma of the Small Intestine (ASI)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	Hairy Cell Leukemia (HCL)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Arm title	Multiple Myeloma (MM)

Arm description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	TMT212 GSK1120212
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A 2 mg once daily tablet administered orally on a continuous basis.

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	DRB436 GSK2118436
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

A 150 mg twice daily capsule administered orally on a continuous basis.

Number of subjects in period 1	Anaplastic Thyroid Cancer (ATC)	Biliary Tract Cancer (BTC)	Gastrointestinal Stromal Tumor (GIST)
Started	36	43	1
Primary analysis cohort	15 [1]	18 [2]	1
Expansion cohort	21 [3]	25 [4]	0 [5]
Completed	24	34	1
Not completed	12	9	0
Consent withdrawn by subject	5	7	-
Physician decision	-	-	-
Study closed by sponsor	6	2	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Low Grade (WHO G1/G2) Glioma (LGG)	High Grade (WHO G3/G4) Glioma (HGG)	Adenocarcinoma of the Small Intestine (ASI)
Started	13	45	3
Primary analysis cohort	13	24 [6]	3
Expansion cohort	0 [7]	21 [8]	0 [9]
Completed	4	28	3
Not completed	9	17	0
Consent withdrawn by subject	3	7	-
Physician decision	-	2	-
Study closed by sponsor	6	7	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Hairy Cell Leukemia (HCL)	Multiple Myeloma (MM)
Started	55	10
Primary analysis cohort	24	10
Expansion cohort	31	0 [10]
Completed	8	9
Not completed	47	1
Consent withdrawn by subject	3	1
Physician decision	1	-
Study closed by sponsor	42	-
Lost to follow-up	1	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.
[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.
[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: For each histology, up to 25 patients were planned to be enrolled in each of the analysis cohorts. A cohort could be closed or stopped early (prior to capping at 25 patients) for futility or efficacy. An uncapped expansion cohort was planned when a particular cohort was stopped early for efficacy.

Baseline characteristics

Reporting groups	
Reporting group title	Anaplastic Thyroid Cancer (ATC)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Biliary Tract Cancer (BTC)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Gastrointestinal Stromal Tumor (GIST)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Low Grade (WHO G1/G2) Glioma (LGG)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	High Grade (WHO G3/G4) Glioma (HGG)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Adenocarcinoma of the Small Intestine (ASI)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Hairy Cell Leukemia (HCL)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Multiple Myeloma (MM)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	

Reporting group values	Anaplastic Thyroid Cancer (ATC)	Biliary Tract Cancer (BTC)	Gastrointestinal Stromal Tumor (GIST)
Number of subjects	36	43	1
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)	9	29	0
From 65-84 years	25	14	1
85 years and over	2	0	0

Age Continuous Units: Years			
arithmetic mean	69.6	57.0	77.0
standard deviation	± 9.53	± 11.88	± 999
Sex: Female, Male Units: Participants			
Female	20	24	1
Male	16	19	0
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	0	0	0
American Indian or Alaska Native	0	0	0
Asian - Central/South Asian Heritage	1	0	0
Asian - East Asian Heritage	11	1	0
Asian - Japanese Heritage	2	2	0
Asian - South East Asian Heritage	2	0	0
White - Arabic/North African Heritage	1	1	0
White - White/Caucasian/European heritage	17	39	1
Missing	2	0	0
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work; 2 = ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours			
Units: Subjects			
Grade 0	4	17	1
Grade 1	30	24	0
Grade 2	2	2	0

Reporting group values	Low Grade (WHO G1/G2) Glioma (LGG)	High Grade (WHO G3/G4) Glioma (HGG)	Adenocarcinoma of the Small Intestine (ASI)
Number of subjects	13	45	3
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	43	3
From 65-84 years	0	2	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	33.1	41.9	58.3
standard deviation	± 11.51	± 14.70	± 3.21

Sex: Female, Male Units: Participants			
Female	9	22	1
Male	4	23	2
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	0	2	1
American Indian or Alaska Native	0	1	0
Asian - Central/South Asian Heritage	0	0	0
Asian - East Asian Heritage	0	4	0
Asian - Japanese Heritage	2	1	0
Asian - South East Asian Heritage	1	1	0
White - Arabic/North African Heritage	0	2	0
White - White/Caucasian/European heritage	10	32	2
Missing	0	2	0
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work; 2 = ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours			
Units: Subjects			
Grade 0	5	14	3
Grade 1	7	24	0
Grade 2	1	7	0

Reporting group values	Hairy Cell Leukemia (HCL)	Multiple Myeloma (MM)	Total
Number of subjects	55	10	206
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)	21	4	122
From 65-84 years	33	6	81
85 years and over	1	0	3
Age Continuous Units: Years			
arithmetic mean	64.8	66.9	
standard deviation	± 10.77	± 6.89	-
Sex: Female, Male Units: Participants			
Female	8	5	90
Male	47	5	116

Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	0	1	4
American Indian or Alaska Native	0	0	1
Asian - Central/South Asian Heritage	0	0	1
Asian - East Asian Heritage	0	1	17
Asian - Japanese Heritage	0	0	7
Asian - South East Asian Heritage	0	0	4
White - Arabic/North African Heritage	1	0	5
White - White/Caucasian/European heritage	48	8	157
Missing	6	0	10
ECOG Performance Status			
The Eastern Cooperative Oncology Group Performance Status (ECOG PS) score classifies participants according to their functional impairment, with scores ranging from 0 (fully active) to 5 (dead). ECOG PS: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work; 2 = ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours			
Units: Subjects			
Grade 0	25	3	72
Grade 1	27	6	118
Grade 2	3	1	16

End points

End points reporting groups

Reporting group title	Anaplastic Thyroid Cancer (ATC)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Biliary Tract Cancer (BTC)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Gastrointestinal Stromal Tumor (GIST)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Low Grade (WHO G1/G2) Glioma (LGG)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	High Grade (WHO G3/G4) Glioma (HGG)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Adenocarcinoma of the Small Intestine (ASI)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Hairy Cell Leukemia (HCL)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	
Reporting group title	Multiple Myeloma (MM)
Reporting group description:	
All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.	

Primary: Overall Response Rate (ORR) in the Anaplastic Thyroid Cancer (ATC) cohort

End point title	Overall Response Rate (ORR) in the Anaplastic Thyroid Cancer (ATC) cohort[1][2]
End point description:	
Overall Response Rate (ORR) was defined as the percentage of participants with a tumor response (complete response [CR], partial response [PR]) by investigator assessment as defined by RECIST v1.1. Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) for target lesions and assessed by MRI: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Overall Response (OR) = CR + PR.	
End point type	Primary
End point timeframe:	
From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Anaplastic Thyroid Cancer (ATC)			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ up to 78 months	56 (38.1 to 72.1)			
Investigator assessment @ up to 92 months	56 (38.1 to 72.1)			
Independent radiology review @ up to 78 months	53 (35.5 to 69.6)			
Independent radiology review @ up to 92 months	53 (35.5 to 69.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the Biliary Tract Cancer (BTC) cohort

End point title	Overall Response Rate (ORR) in the Biliary Tract Cancer (BTC) cohort[3][4]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with a tumor response (complete response [CR], partial response [PR]) by investigator assessment as defined by RECIST v1.1. Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) for target lesions and assessed by MRI: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Overall Response (OR) = CR + PR.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Biliary Tract Cancer (BTC)			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ up to 78 months	53 (37.7 to 68.8)			
Investigator assessment @ up to 92 months	53 (37.7 to 68.8)			
Independent radiology review @ up to 78 months	47 (31.2 to 62.3)			
Independent radiology review @ up to 92 months	47 (31.2 to 62.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the Gastrointestinal Stromal Tumor (GIST) cohort

End point title	Overall Response Rate (ORR) in the Gastrointestinal Stromal Tumor (GIST) cohort[5][6]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with a tumor response (complete response [CR], partial response [PR]) by investigator assessment as defined by RECIST v1.1. Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) for target lesions and assessed by MRI: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Overall Response (OR) = CR + PR.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Gastrointestinal Stromal Tumor (GIST)			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ 78 months	(to)			
Investigator assessment @ 92 months	(to)			

Notes:

[7] - insufficient number of participants with events.

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the Adenocarcinoma of the Small Intestine (ASI) cohort

End point title	Overall Response Rate (ORR) in the Adenocarcinoma of the Small Intestine (ASI) cohort[8][9]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with a tumor response (complete response [CR], partial response [PR]) by investigator assessment as defined by RECIST v1.1. Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) for target lesions and assessed by MRI: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Overall Response (OR) = CR + PR.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Adenocarcinoma of the Small Intestine (ASI)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ up to 78 months	67 (9.4 to 99.2)			
Investigator assessment @ up to 92 months	67 (9.4 to 99.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort

End point title	Overall Response Rate (ORR) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort[10][11]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with a tumor response (response assessment criteria (CR, PR, and minor response [MR]) WHO Grade 1 and 2 Glioma) by investigator assessment as defined by response assessment for neuro-oncology (RANO). Specifically, ORR = number of subjects with a confirmed overall response divided by the total number of subjects in the corresponding analysis population.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Low Grade (WHO G1/G2) Glioma (LGG)			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Percentage of Participants				
number (confidence interval 95%)				
Inv. assessment/Response rate @ up to 78 months	69 (38.6 to 90.9)			
Inv. assessment/Response rate @ up to 92 months	69 (38.6 to 90.9)			
Indep. Rad. rev./Response rate @ up to 78 months	69 (38.6 to 90.9)			
Indep. Rad. rev./Response rate @ up to 92 months	62 (31.6 to 86.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the High Grade (WHO G3/G4) Glioma (HGG) cohort

End point title	Overall Response Rate (ORR) in the High Grade (WHO G3/G4) Glioma (HGG) cohort[12][13]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with a tumor response (updated response assessment criteria (CR, PR) WHO Grade 3 and 4 Glioma) by investigator assessment as defined by modified response assessment for neuro-oncology (RANO). Specifically, ORR = number of subjects with a confirmed overall response divided by the total number of subjects in the corresponding analysis population.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	High Grade (WHO G3/G4) Glioma (HGG)			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ up to 78 months	33 (20.0 to 49.0)			
Investigator assessment @ up to 92 months	33 (20.0 to 49.0)			
Independent radiology review @ up to 78 months	31 (18.2 to 46.6)			
Independent radiology review @ up to 92 months	31 (18.2 to 46.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the Hairy Cell Leukemia (HCL) cohort

End point title	Overall Response Rate (ORR) in the Hairy Cell Leukemia (HCL) cohort[14][15]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with CR +/- minimal residual disease [MRD], PR by investigator assessment as defined by the Consensus Resolution Criteria adapted from the National Comprehensive Cancer Network (NCCN) guidelines. Specifically, ORR = number of subjects with a confirmed overall response divided by the total number of subjects in the corresponding analysis population.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Hairy Cell Leukemia (HCL)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ up to 78 months	89 (77.8 to 95.9)			
Investigator assessment @ up to 92 months	89 (77.8 to 95.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) in the Multiple Myeloma (MM) cohort

End point title	Overall Response Rate (ORR) in the Multiple Myeloma (MM) cohort[16][17]

End point description:

Overall Response Rate (ORR) was defined as the percentage of participants with stringent complete response (sCR), CR, PR, very good partial response (VGPR) by investigator assessment as defined by the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma. Specifically, ORR = number of subjects with a confirmed overall response divided by the total number of subjects in the corresponding analysis population.

End point type	Primary

End point timeframe:

From study treatment start date until first documented complete response or partial response, assessed up to 78 months (cut-off date for FDA Submission = 14-Sep-20) and up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis performed

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Multiple Myeloma (MM)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of Participants				
number (confidence interval 95%)				
Investigator assessment @ up to 78 months	50 (18.7 to 81.3)			
Investigator assessment @ up to 92 months	50 (18.7 to 81.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the Anaplastic Thyroid Cancer (ATC) cohort

End point title	Duration of Response (DoR) in the Anaplastic Thyroid Cancer (ATC) cohort[18]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Anaplastic Thyroid Cancer (ATC)			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	62.4 (32.1 to 999)			
Independent radiology review	59.1 (16.6 to 171.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the Biliary Tract Cancer (BTC) cohort

End point title	Duration of Response (DoR) in the Biliary Tract Cancer (BTC) cohort[19]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Biliary Tract Cancer (BTC)			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	38.9 (24.3 to 59.4)			
Independent radiology review	45.4 (20.1 to 64.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the High Grade (WHO G3/G4) Glioma (HGG) cohort

End point title	Duration of Response (DoR) in the High Grade (WHO G3/G4) Glioma (HGG) cohort[20]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	High Grade (WHO G3/G4) Glioma (HGG)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	135.7 (32.0 to 192.0)			
Independent radiology review	59.3 (20.1 to 116.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort

End point title	Duration of Response (DoR) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort[21]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Low Grade (WHO G1/G2) Glioma (LGG)			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	999 (24.1 to 999)			
Independent radiology review	84.3 (16.4 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the Adenocarcinoma of the Small Intestine (ASI) cohort

End point title	Duration of Response (DoR) in the Adenocarcinoma of the Small Intestine (ASI) cohort[22]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of

Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Adenocarcinoma of the Small Intestine (ASI)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	999 (999 to 999)			
Independent radiology review	32.8 (32.1 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the Hairy Cell Leukemia (HCL) cohort

End point title	Duration of Response (DoR) in the Hairy Cell Leukemia (HCL) cohort[23]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Hairy Cell Leukemia (HCL)			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: Weeks				
median (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) in the Multiple Myeloma (MM) cohort

End point title	Duration of Response (DoR) in the Multiple Myeloma (MM) cohort[24]

End point description:

For the subset of subjects who showed a confirmed response as defined for each cohort, Duration of Response (DoR) was defined as the time (in weeks) from first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever was first. If the subject did not have a documented date of progression or death, DoR was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From first documented evidence of response (the first response prior to confirmation) until time of documented disease progression or death due to any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Multiple Myeloma (MM)			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Weeks				
median (confidence interval 95%)	48.1 (24.3 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the Anaplastic Thyroid Cancer (ATC) cohort

End point title	Progression Free Survival (PFS) in the Anaplastic Thyroid Cancer (ATC) cohort[25]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment

and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1), as a 20% increase in the sum of the diameters of target lesions, taking as a reference, the smallest sum of diameters recorded since the treatment started.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Anaplastic Thyroid Cancer (ATC)			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	29.1 (20.3 to 59.9)			
Independent radiology review	24.1 (16.1 to 56.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the Biliary Tract Cancer (BTC) cohort

End point title	Progression Free Survival (PFS) in the Biliary Tract Cancer (BTC) cohort[26]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1), as a 20% increase in the sum of the diameters of target lesions, taking as a reference, the smallest sum of diameters recorded since the treatment started.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Biliary Tract Cancer (BTC)			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	39.0 (24.1 to 41.0)			
Independent radiology review	32.6 (23.6 to 56.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the Adenocarcinoma of the Small Intestine (ASI) cohort

End point title	Progression Free Survival (PFS) in the Adenocarcinoma of the Small Intestine (ASI) cohort[27]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1), as a 20% increase in the sum of the diameters of target lesions, taking as a reference, the smallest sum of diameters recorded since the treatment started.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Adenocarcinoma of the Small Intestine (ASI)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	999 (999 to 999)			
Independent radiology review	40.1 (4.1 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the Hairy Cell Leukemia (HCL) cohort

End point title	Progression Free Survival (PFS) in the Hairy Cell Leukemia (HCL) cohort[28]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Hairy Cell Leukemia (HCL)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Weeks				
median (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the High Grade (WHO G3/G4) Glioma (HGG) cohort

End point title	Progression Free Survival (PFS) in the High Grade (WHO G3/G4) Glioma (HGG) cohort[29]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	High Grade (WHO G3/G4) Glioma (HGG)			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	24.0 (8.0 to 59.4)			
Independent radiology review	19.7 (8.0 to 32.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort

End point title	Progression Free Survival (PFS) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort[30]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Low Grade (WHO G1/G2) Glioma (LGG)			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Weeks				
median (confidence interval 95%)				
Investigator assessment	999 (32.1 to 999)			
Independent radiology review	40.1 (20.3 to 143.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the Hairy Cell Leukemia (HCL) cohort

End point title	Overall Survival (OS) in the Hairy Cell Leukemia (HCL)

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Hairy Cell Leukemia (HCL)			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Weeks				
median (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the Multiple Myeloma (MM) cohort

End point title	Overall Survival (OS) in the Multiple Myeloma (MM) cohort[32]

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Multiple Myeloma (MM)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Weeks				
median (confidence interval 95%)	147.3 (12.4 to 194.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in the Multiple Myeloma (MM) cohort

End point title	Progression Free Survival (PFS) in the Multiple Myeloma (MM) cohort[33]

End point description:

Progression Free Survival (PFS) was defined as the interval between the first dose of study treatment and earlier date of first radiologically documented progression or death due to any cause. If the subject did not have a documented date of progression or death, PFS was censored at the date of the last adequate assessment.

End point type	Secondary

End point timeframe:

From study treatment start date until date of radiographic progression or date of death from any cause, whichever comes first, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Multiple Myeloma (MM)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Weeks				
median (confidence interval 95%)	27.5 (10.0 to 55.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the Anaplastic Thyroid Cancer (ATC) cohort

End point title	Overall Survival (OS) in the Anaplastic Thyroid Cancer (ATC) cohort[34]

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Anaplastic Thyroid Cancer (ATC)			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Weeks				
median (confidence interval 95%)	62.9 (29.6 to 100.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the Biliary Tract Cancer (BTC) cohort

End point title	Overall Survival (OS) in the Biliary Tract Cancer (BTC)

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Biliary Tract Cancer (BTC)			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Weeks				
median (confidence interval 95%)	58.9 (45.4 to 76.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the Adenocarcinoma of the Small Intestine (ASI) cohort

End point title	Overall Survival (OS) in the Adenocarcinoma of the Small

	Intestine (ASI) cohort[36]

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Adenocarcinoma of the Small Intestine (ASI)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Weeks				
median (confidence interval 95%)	94.6 (14.9 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort

End point title	Overall Survival (OS) in the Low Grade (WHO G1/G2) Glioma (LGG) cohort[37]

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	Low Grade (WHO G1/G2) Glioma (LGG)			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Weeks				
median (confidence interval 95%)	999 (50.4 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in the High Grade (WHO G3/G4) Glioma (HGG) cohort

End point title	Overall Survival (OS) in the High Grade (WHO G3/G4) Glioma (HGG) cohort[38]

End point description:

Overall Survival (OS) was defined as the time from first dose until death due to any cause. Censoring was performed using the date of last known contact for those who were alive at the time of analysis.

End point type	Secondary

End point timeframe:

From study treatment start date until date of death from any cause, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects were enrolled into cohorts based on the type of histology. Each histology is presented as a distinct arm in the endpoints

End point values	High Grade (WHO G3/G4) Glioma (HGG)			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Weeks				
median (confidence interval 95%)	76.4 (41.1 to 139.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)

End point description:

The distribution of adverse events (AE) was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs) and Serious Adverse Event (TESAEs) through the monitoring of relevant clinical and laboratory safety parameters.

End point type	Secondary

End point timeframe:

From study treatment start date till 30 days safety follow-up, assessed up to 92 months (cut-off date for end of study = 10-Dec-21)

End point values	Anaplastic Thyroid Cancer (ATC)	Biliary Tract Cancer (BTC)	Gastrointestinal Stromal Tumor (GIST)	Low Grade (WHO G1/G2) Glioma (LGG)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	43	1	13
Units: Participants				
Any AE	36	43	1	12
AEs related to study treatment	27	42	1	12
AEs leading to permanent disc. of any study tx	6	1	0	2
AEs leading to dose reduction	17	15	1	4
AEs leading to dose interruption/delay	19	24	1	6
Any SAE	20	17	1	3
SAEs related to study treatment	7	9	0	1
Fatal SAEs	3	2	0	0

End point values	High Grade (WHO G3/G4) Glioma (HGG)	Adenocarcinoma of the Small Intestine (ASI)	Hairy Cell Leukemia (HCL)	Multiple Myeloma (MM)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	3	55	10
Units: Participants				
Any AE	42	3	55	9
AEs related to study treatment	37	3	52	7
AEs leading to permanent disc. of any study tx	4	1	13	1
AEs leading to dose reduction	18	2	29	5
AEs leading to dose interruption/delay	18	2	40	6
Any SAE	16	0	32	4
SAEs related to study treatment	7	0	19	3
Fatal SAEs	1	0	3	0

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

On-treatment deaths were collected from first dose of study medication to 30 days after study drug discontinuation, for a maximum duration of 85 months. Post-treatment survival follow-up deaths were collected from day 31 after last dose of first dose of study medication, up to 92 months. All deaths refer to the sum of on-treatment deaths and post-treatment survival follow-up deaths.

End point type	Post-hoc

End point timeframe:

On-treatment deaths: Up to 85 months. Post-treatment survival follow-up deaths: Up to 92 months.

End point values	Anaplastic Thyroid Cancer (ATC)	Biliary Tract Cancer (BTC)	Gastrointestinal Stromal Tumor (GIST)	Low Grade (WHO G1/G2) Glioma (LGG)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	43	1	13
Units: Participants				
On-treatment deaths	6	6	0	1
Post-treatment survival follow-up deaths	18	28	1	3
All deaths	24	34	1	4

End point values	High Grade (WHO G3/G4) Glioma (HGG)	Adenocarcinoma of the Small Intestine (ASI)	Hairy Cell Leukemia (HCL)	Multiple Myeloma (MM)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	3	55	10
Units: Participants				
On-treatment deaths	2	0	4	1
Post-treatment survival follow-up deaths	26	3	4	8
All deaths	28	3	8	9

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days, up to approximately 85 months (study treatment with dabrafenib and trametinib ranged from 1 to 84 months).

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Anaplastic Thyroid Cancer (ATC)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Biliary Tract Cancer (BTC)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Gastrointestinal Stromal Tumor (GIST)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Low Grade (WHO G1/G2) Glioma (LGG)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Total

Reporting group description:

All subjects enrolled in the study received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Adenocarcinoma of the Small Intestine (ASI)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Hairy Cell Leukemia (HCL)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	Multiple Myeloma (MM)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Reporting group title	High Grade (WHO G3/G4) Glioma (HGG)

Reporting group description:

All subjects enrolled received oral dabrafenib 150 mg bid in combination with oral trametinib 2 mg once daily. Subjects continued treatment until an unacceptable toxicity, disease progression, or death.

Serious adverse events	Anaplastic Thyroid Cancer (ATC)	Biliary Tract Cancer (BTC)	Gastrointestinal Stromal Tumor (GIST)
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 36 (55.56%)	17 / 43 (39.53%)	1 / 1 (100.00%)
number of deaths (all causes)	6	6	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Bowen's disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Bladder neoplasm			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Chronic lymphocytic leukaemia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Metastases to bone			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Invasive breast carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Hodgkin's disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Prostate cancer			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Aortic thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Thrombophlebitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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			
Fatigue			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Fat necrosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Chills			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
General physical health deterioration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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

Pyrexia			
subjects affected / exposed	1 / 36 (2.78%)	9 / 43 (20.93%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 4	10 / 13	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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			
Aspiration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Pulmonary granuloma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Pulmonary embolism			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Pneumothorax			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Pleural effusion			
subjects affected / exposed	3 / 36 (8.33%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Pulmonary haematoma			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Psychiatric disorders			
Hallucination			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Product issues			
Device failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Ejection fraction decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
White blood cell count decreased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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

Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Contusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Fall			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Femoral neck fracture			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural discomfort			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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

Conduction disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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 ventricular thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Atrioventricular block			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Stress cardiomyopathy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Myocarditis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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			
Aphasia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Amnesia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Ataxia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Dizziness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Cerebral thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Cerebral cyst			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Central nervous system lesion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Brain oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Headache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Guillain-Barre syndrome			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Facial nerve disorder			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Epilepsy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Syncope			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Seizure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Paralysis recurrent laryngeal nerve			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Haemolytic uraemic syndrome			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Febrile neutropenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Leukopenia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Retinal detachment			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Diplopia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Dysphagia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Oesophageal stenosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Large intestinal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Intestinal obstruction			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Cholangitis			
subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Skin and subcutaneous tissue disorders			

Skin ulcer			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Erythema nodosum			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Renal colic			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Haematuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Calculus urinary			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Acute kidney injury			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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

Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Muscular weakness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Neck pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Spinal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Infections and infestations			
Cervicitis human papilloma virus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Cellulitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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

Bacterial diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Clostridium difficile infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Gastroenteritis pseudomonas			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Enterobacter infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Diverticulitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Device related infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Pelvic infection			

subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Parotitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Otitis media acute			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Lymph node tuberculosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Influenza			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Pneumonia			
subjects affected / exposed	8 / 36 (22.22%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 11	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Pulmonary sepsis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Pneumonia necrotising			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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 aspiration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Staphylococcal infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Viral infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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			

subjects affected / exposed	1 / 36 (2.78%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Wound infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (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
Dehydration			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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
Hyponatraemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (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	Low Grade (WHO G1/G2) Glioma (LGG)	Total	Adenocarcinoma of the Small Intestine (ASI)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 13 (23.08%)	93 / 206 (45.15%)	0 / 3 (0.00%)
number of deaths (all causes)	1	20	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Bowen's disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Bladder neoplasm			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Metastases to bone			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Invasive breast carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Hodgkin's disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 14	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic thrombosis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Thrombophlebitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fat necrosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Chills			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	23 / 206 (11.17%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	26 / 38	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pulmonary granuloma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pulmonary embolism			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pulmonary haematoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Psychiatric disorders			
Hallucination			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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

Product issues			
Device failure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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			
Neutrophil count decreased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Contusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Femoral neck fracture			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Conduction disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Atrioventricular block			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Stress cardiomyopathy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Myocarditis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Amnesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Ataxia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral thrombosis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Cerebral cyst			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Central nervous system lesion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Brain oedema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Headache			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Guillain-Barre syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Facial nerve disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			

subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Seizure			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paralysis recurrent laryngeal nerve			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Febrile neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Leukopenia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Retinal detachment			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Diplopia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Constipation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Large intestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Intestinal obstruction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Haematochezia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Cholangitis			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Erythema nodosum			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Renal and urinary disorders			

Urinary retention			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Renal colic			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Acute kidney injury			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenocortical insufficiency acute			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Muscular weakness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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

Musculoskeletal chest pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Neck pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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			
Cervicitis human papilloma virus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Cellulitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Bacteraemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Clostridium difficile infection			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis pseudomonas			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Enterobacter infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Diverticulitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Device related infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pelvic infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Parotitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Otitis media acute			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Lymph node tuberculosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Influenza			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	13 / 206 (6.31%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 18	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pneumonia necrotising			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Pneumonia aspiration			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Staphylococcal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Viral infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 4	0 / 0
Wound infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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
Hyponatraemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (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

Serious adverse events	Hairy Cell Leukemia (HCL)	Multiple Myeloma (MM)	High Grade (WHO G3/G4) Glioma (HGG)
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 55 (58.18%)	4 / 10 (40.00%)	16 / 45 (35.56%)
number of deaths (all causes)	4	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Bladder neoplasm			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	5 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Metastatic squamous cell carcinoma			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Metastases to bone			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Invasive breast carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hodgkin's disease			

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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 stromal tumour			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	3 / 14	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Aortic thrombosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Thrombophlebitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fat necrosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	2 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	10 / 55 (18.18%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	10 / 17	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Pulmonary granuloma			

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Pulmonary embolism			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Pleural effusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Dyspnoea			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Pulmonary haematoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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			
Hallucination			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Product issues			
Device failure			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Investigations			

Neutrophil count decreased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Transaminases increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Contusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Femoral neck fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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

Rib fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Post procedural discomfort			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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 disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Conduction disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Atrioventricular block			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Myocardial ischaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Stress cardiomyopathy			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Myocarditis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Amnesia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Ataxia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral thrombosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Guillain-Barre syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Facial nerve disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Hydrocephalus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Epilepsy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Seizure			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paralysis recurrent laryngeal nerve			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Febrile neutropenia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Leukopenia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Neutropenia			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Retinal detachment			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (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
Diplopia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (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
Constipation			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Abdominal pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Nausea			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	3 / 45 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Large intestinal haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Intestinal obstruction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Haematochezia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Vomiting			

subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	3 / 45 (6.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Hepatotoxicity			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Erythema nodosum			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Renal colic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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

Haematuria			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Acute kidney injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Endocrine disorders			
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Muscular weakness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Neck pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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

Spinal pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Infections and infestations			
Cervicitis human papilloma virus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial diarrhoea			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Bacteraemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Infection			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis pseudomonas			

subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Enterobacter infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (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
Diverticulitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Device related infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Pelvic infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Parotitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Otitis media acute			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Lymph node tuberculosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (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
Pneumonia			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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 necrotising			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (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
Urinary tract infection			

subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	2 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Staphylococcal infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Viral infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Wound infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Dehydration			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (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
Hyperglycaemic hyperosmolar nonketotic syndrome			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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
Hyponatraemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (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

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

Non-serious adverse events	Anaplastic Thyroid Cancer (ATC)	Biliary Tract Cancer (BTC)	Gastrointestinal Stromal Tumor (GIST)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 36 (100.00%)	43 / 43 (100.00%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic keratosis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Melanocytic naevus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lipoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fibroma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Basal cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Vascular disorders			

Lymphoedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	5 / 36 (13.89%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Hypertension			
subjects affected / exposed	1 / 36 (2.78%)	6 / 43 (13.95%)	0 / 1 (0.00%)
occurrences (all)	1	6	0
Hot flush			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Varicose vein			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 36 (36.11%)	14 / 43 (32.56%)	0 / 1 (0.00%)
occurrences (all)	20	17	0
Asthenia			
subjects affected / exposed	3 / 36 (8.33%)	7 / 43 (16.28%)	1 / 1 (100.00%)
occurrences (all)	4	9	1
Chills			
subjects affected / exposed	8 / 36 (22.22%)	12 / 43 (27.91%)	0 / 1 (0.00%)
occurrences (all)	14	21	0
Feeling cold			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Gait disturbance			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Influenza like illness			

subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Injection site reaction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	5 / 36 (13.89%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	6	4	0
Mucosal inflammation			
subjects affected / exposed	3 / 36 (8.33%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	3	4	0
Nodule			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Oedema			
subjects affected / exposed	1 / 36 (2.78%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Malaise			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	17 / 36 (47.22%)	25 / 43 (58.14%)	1 / 1 (100.00%)
occurrences (all)	35	56	7
Thirst			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Xerosis			

subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Sarcoidosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	8 / 36 (22.22%)	7 / 43 (16.28%)	0 / 1 (0.00%)
occurrences (all)	9	7	0
Dysphonia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hiccups			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	4 / 36 (11.11%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Epistaxis			
subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Cough			
subjects affected / exposed	4 / 36 (11.11%)	10 / 43 (23.26%)	0 / 1 (0.00%)
occurrences (all)	4	11	0
Lung disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			

subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Rhinitis allergic			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Pulmonary embolism			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Pleural effusion			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Nasal congestion			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Productive cough			
subjects affected / exposed	3 / 36 (8.33%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Wheezing			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Anxiety			
subjects affected / exposed	1 / 36 (2.78%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Agitation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Emotional disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	5 / 36 (13.89%)	6 / 43 (13.95%)	0 / 1 (0.00%)
occurrences (all)	5	6	0
Libido decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Alanine aminotransferase increased			
subjects affected / exposed	4 / 36 (11.11%)	7 / 43 (16.28%)	0 / 1 (0.00%)
occurrences (all)	6	12	0
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 36 (13.89%)	11 / 43 (25.58%)	0 / 1 (0.00%)
occurrences (all)	8	18	0
Blood alkaline phosphatase increased			

subjects affected / exposed	6 / 36 (16.67%)	9 / 43 (20.93%)	0 / 1 (0.00%)
occurrences (all)	8	12	0
Blood bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Blood creatinine increased			
subjects affected / exposed	2 / 36 (5.56%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	3	6	0
Blood glucose increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Blood oestrogen decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	3 / 36 (8.33%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Blood urea increased			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood testosterone decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 36 (8.33%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0

Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 36 (8.33%)	12 / 43 (27.91%)	0 / 1 (0.00%)
occurrences (all)	5	13	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Lipase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	1 / 36 (2.78%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	4	9	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Neutrophil count decreased			
subjects affected / exposed	3 / 36 (8.33%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	4	4	0
Neutrophil count increased			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Liver function test increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	4 / 36 (11.11%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	4	3	0
Weight increased			
subjects affected / exposed	1 / 36 (2.78%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	1	4	0
White blood cell count decreased			

subjects affected / exposed	5 / 36 (13.89%)	10 / 43 (23.26%)	0 / 1 (0.00%)
occurrences (all)	15	16	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Procedural pain			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Radiation associated pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Atrial fibrillation			

subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Epilepsy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Dizziness			
subjects affected / exposed	7 / 36 (19.44%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	7	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Head discomfort			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	8 / 36 (22.22%)	10 / 43 (23.26%)	0 / 1 (0.00%)
occurrences (all)	10	12	0
Hemiparesis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hydrocephalus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Facial paresis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Intercostal neuralgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
IIIrd nerve disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	2 / 36 (5.56%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Palatal palsy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0

Pyramidal tract syndrome			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
VIth nerve disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Anaemia			
subjects affected / exposed	12 / 36 (33.33%)	10 / 43 (23.26%)	0 / 1 (0.00%)
occurrences (all)	14	11	0
Lymphopenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Microcytic anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Thrombocytopenia			
subjects affected / exposed	2 / 36 (5.56%)	7 / 43 (16.28%)	0 / 1 (0.00%)
occurrences (all)	4	12	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Hypoacusis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Cataract			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Diplopia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Iritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Papilloedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Photophobia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Saccadic eye movement			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	4 / 36 (11.11%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Vitreous floaters			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	7 / 36 (19.44%)	14 / 43 (32.56%)	0 / 1 (0.00%)
occurrences (all)	12	19	0
Abdominal pain lower			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 36 (5.56%)	7 / 43 (16.28%)	0 / 1 (0.00%)
occurrences (all)	2	9	0
Constipation			

subjects affected / exposed	8 / 36 (22.22%)	9 / 43 (20.93%)	1 / 1 (100.00%)
occurrences (all)	8	10	1
Abdominal pain			
subjects affected / exposed	2 / 36 (5.56%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	2	5	0
Dry mouth			
subjects affected / exposed	5 / 36 (13.89%)	8 / 43 (18.60%)	0 / 1 (0.00%)
occurrences (all)	7	8	0
Dyspepsia			
subjects affected / exposed	1 / 36 (2.78%)	3 / 43 (6.98%)	1 / 1 (100.00%)
occurrences (all)	5	3	1
Dysphagia			
subjects affected / exposed	6 / 36 (16.67%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Flatulence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Noninfective gingivitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	12 / 36 (33.33%)	18 / 43 (41.86%)	1 / 1 (100.00%)
occurrences (all)	17	27	1
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 36 (8.33%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	3	3	0
Oral pain			

subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Retching			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Salivary gland mass			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	2 / 36 (5.56%)	3 / 43 (6.98%)	1 / 1 (100.00%)
occurrences (all)	3	3	5
Vomiting			
subjects affected / exposed	7 / 36 (19.44%)	15 / 43 (34.88%)	1 / 1 (100.00%)
occurrences (all)	8	31	5
Toothache			
subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 36 (0.00%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Dry skin			
subjects affected / exposed	4 / 36 (11.11%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	4	4	0
Dermatitis acneiform			
subjects affected / exposed	1 / 36 (2.78%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	2	7	0
Alopecia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Actinic keratosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0

Erythema			
subjects affected / exposed	1 / 36 (2.78%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	1	5	0
Erythema nodosum			
subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Hyperkeratosis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hyperhidrosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hidradenitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Piloerection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	3 / 36 (8.33%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	4	3	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Papule			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nail discolouration			

subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	3 / 36 (8.33%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	3	5	0
Rash			
subjects affected / exposed	10 / 36 (27.78%)	12 / 43 (27.91%)	0 / 1 (0.00%)
occurrences (all)	13	14	0
Pruritus			
subjects affected / exposed	4 / 36 (11.11%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	6	5	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin striae			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin plaque			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Skin lesion			
subjects affected / exposed	2 / 36 (5.56%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin atrophy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Chromaturia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Pollakiuria			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Renal failure			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	4 / 36 (11.11%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Joint stiffness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Arthralgia			

subjects affected / exposed	5 / 36 (13.89%)	6 / 43 (13.95%)	0 / 1 (0.00%)
occurrences (all)	8	8	0
Arthritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	6 / 36 (16.67%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	6	5	0
Bone pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Foot deformity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	1	5	0
Neck pain			
subjects affected / exposed	3 / 36 (8.33%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Neck mass			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Myalgia			

subjects affected / exposed	2 / 36 (5.56%)	8 / 43 (18.60%)	0 / 1 (0.00%)
occurrences (all)	2	9	0
Musculoskeletal pain			
subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Muscular weakness			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Myopathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abdominal abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0

Folliculitis			
subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Nasopharyngitis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Gingivitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 36 (0.00%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Onychomycosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	2	1	0

Pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rash pustular			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Skin candida			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Streptococcal infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 36 (8.33%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	2	2	0

Tooth abscess			
subjects affected / exposed	0 / 36 (0.00%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	12 / 36 (33.33%)	10 / 43 (23.26%)	0 / 1 (0.00%)
occurrences (all)	15	12	0
Dehydration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	3 / 36 (8.33%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Hyperglycaemia			
subjects affected / exposed	5 / 36 (13.89%)	8 / 43 (18.60%)	0 / 1 (0.00%)
occurrences (all)	5	9	0
Hyperkalaemia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 43 (2.33%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Hyperuricaemia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Hypoalbuminaemia			
subjects affected / exposed	7 / 36 (19.44%)	3 / 43 (6.98%)	0 / 1 (0.00%)
occurrences (all)	7	6	0
Hypocalcaemia			
subjects affected / exposed	5 / 36 (13.89%)	0 / 43 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Hypophosphataemia			

subjects affected / exposed	1 / 36 (2.78%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	4 / 36 (11.11%)	4 / 43 (9.30%)	0 / 1 (0.00%)
occurrences (all)	4	8	0
Hypomagnesaemia			
subjects affected / exposed	2 / 36 (5.56%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	2	10	0
Hyponatraemia			
subjects affected / exposed	7 / 36 (19.44%)	5 / 43 (11.63%)	0 / 1 (0.00%)
occurrences (all)	11	8	0
Hypoglycaemia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 43 (4.65%)	0 / 1 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Low Grade (WHO G1/G2) Glioma (LGG)	Total	Adenocarcinoma of the Small Intestine (ASI)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)	201 / 206 (97.57%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Seborrhoeic keratosis			
subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Melanocytic naevus			
subjects affected / exposed	2 / 13 (15.38%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Lipoma			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Fibroma			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Basal cell carcinoma			

subjects affected / exposed	0 / 13 (0.00%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	0	25	0
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypotension			
subjects affected / exposed	2 / 13 (15.38%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	3	18	0
Hypertension			
subjects affected / exposed	2 / 13 (15.38%)	21 / 206 (10.19%)	1 / 3 (33.33%)
occurrences (all)	3	26	1
Hot flush			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Flushing			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	1 / 3 (33.33%)
occurrences (all)	1	10	1
Varicose vein			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 13 (61.54%)	86 / 206 (41.75%)	0 / 3 (0.00%)
occurrences (all)	9	148	0
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	19 / 206 (9.22%)	0 / 3 (0.00%)
occurrences (all)	0	27	0
Chills			
subjects affected / exposed	3 / 13 (23.08%)	61 / 206 (29.61%)	1 / 3 (33.33%)
occurrences (all)	5	195	1
Feeling cold			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Gait disturbance			

subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Influenza like illness			
subjects affected / exposed	2 / 13 (15.38%)	13 / 206 (6.31%)	0 / 3 (0.00%)
occurrences (all)	2	18	0
Injection site reaction			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Oedema peripheral			
subjects affected / exposed	2 / 13 (15.38%)	44 / 206 (21.36%)	1 / 3 (33.33%)
occurrences (all)	3	63	1
Mucosal inflammation			
subjects affected / exposed	1 / 13 (7.69%)	12 / 206 (5.83%)	0 / 3 (0.00%)
occurrences (all)	2	14	0
Nodule			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Non-cardiac chest pain			
subjects affected / exposed	3 / 13 (23.08%)	11 / 206 (5.34%)	1 / 3 (33.33%)
occurrences (all)	3	11	1
Oedema			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Malaise			
subjects affected / exposed	2 / 13 (15.38%)	9 / 206 (4.37%)	0 / 3 (0.00%)
occurrences (all)	2	23	0
Pain			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	1 / 3 (33.33%)
occurrences (all)	0	5	1
Peripheral swelling			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Pyrexia			
subjects affected / exposed	8 / 13 (61.54%)	108 / 206 (52.43%)	2 / 3 (66.67%)
occurrences (all)	18	337	3
Thirst			

subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Xerosis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Sarcoidosis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	31 / 206 (15.05%)	0 / 3 (0.00%)
occurrences (all)	0	38	0
Dysphonia			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Hiccups			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Haemoptysis			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Epistaxis			
subjects affected / exposed	1 / 13 (7.69%)	13 / 206 (6.31%)	0 / 3 (0.00%)
occurrences (all)	7	22	0
Cough			
subjects affected / exposed	3 / 13 (23.08%)	56 / 206 (27.18%)	0 / 3 (0.00%)
occurrences (all)	5	88	0
Lung disorder			

subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Rhinitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Pulmonary embolism			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 13 (0.00%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Pneumonitis			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Oropharyngeal pain			
subjects affected / exposed	2 / 13 (15.38%)	16 / 206 (7.77%)	0 / 3 (0.00%)
occurrences (all)	2	20	0
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)	23 / 206 (11.17%)	0 / 3 (0.00%)
occurrences (all)	0	35	0
Productive cough			
subjects affected / exposed	0 / 13 (0.00%)	13 / 206 (6.31%)	0 / 3 (0.00%)
occurrences (all)	0	16	0
Wheezing			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Confusional state			
subjects affected / exposed	2 / 13 (15.38%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences (all)	2	14	0
Anxiety			
subjects affected / exposed	1 / 13 (7.69%)	9 / 206 (4.37%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Agitation			
subjects affected / exposed	2 / 13 (15.38%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Sleep disorder			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Depression			
subjects affected / exposed	2 / 13 (15.38%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	2	10	0
Emotional disorder			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	2 / 13 (15.38%)	26 / 206 (12.62%)	1 / 3 (33.33%)
occurrences (all)	2	26	1
Libido decreased			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Mood swings			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 13 (15.38%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	2	8	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 13 (23.08%)	41 / 206 (19.90%)	0 / 3 (0.00%)
occurrences (all)	3	69	0
Aspartate aminotransferase increased			

subjects affected / exposed	4 / 13 (30.77%)	50 / 206 (24.27%)	0 / 3 (0.00%)
occurrences (all)	4	96	0
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 13 (23.08%)	36 / 206 (17.48%)	0 / 3 (0.00%)
occurrences (all)	7	58	0
Blood bilirubin increased			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Blood creatinine increased			
subjects affected / exposed	0 / 13 (0.00%)	22 / 206 (10.68%)	0 / 3 (0.00%)
occurrences (all)	0	32	0
Blood glucose increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 13 (7.69%)	9 / 206 (4.37%)	0 / 3 (0.00%)
occurrences (all)	1	11	0
Blood oestrogen decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Ejection fraction decreased			
subjects affected / exposed	1 / 13 (7.69%)	17 / 206 (8.25%)	0 / 3 (0.00%)
occurrences (all)	1	24	0
Blood urea increased			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood uric acid increased			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Blood testosterone decreased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 13 (7.69%)	11 / 206 (5.34%)	0 / 3 (0.00%)
occurrences (all)	1	14	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 13 (7.69%)	19 / 206 (9.22%)	0 / 3 (0.00%)
occurrences (all)	1	22	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Lipase increased			
subjects affected / exposed	2 / 13 (15.38%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Platelet count decreased			
subjects affected / exposed	1 / 13 (7.69%)	11 / 206 (5.34%)	0 / 3 (0.00%)
occurrences (all)	1	18	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	2	11	0
Neutrophil count decreased			
subjects affected / exposed	3 / 13 (23.08%)	20 / 206 (9.71%)	0 / 3 (0.00%)
occurrences (all)	5	43	0
Neutrophil count increased			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Liver function test increased			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Urine output decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	13 / 206 (6.31%)	1 / 3 (33.33%)
occurrences (all)	1	13	1
Weight increased			

subjects affected / exposed	3 / 13 (23.08%)	12 / 206 (5.83%)	1 / 3 (33.33%)
occurrences (all)	3	12	1
White blood cell count decreased			
subjects affected / exposed	3 / 13 (23.08%)	27 / 206 (13.11%)	0 / 3 (0.00%)
occurrences (all)	9	66	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 13 (0.00%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	0	11	0
Fall			
subjects affected / exposed	1 / 13 (7.69%)	13 / 206 (6.31%)	0 / 3 (0.00%)
occurrences (all)	1	18	0
Procedural pain			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Radiation associated pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Thermal burn			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Bradycardia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 13 (0.00%)	16 / 206 (7.77%)	0 / 3 (0.00%)
occurrences (all)	0	18	0
Tachycardia			

subjects affected / exposed	1 / 13 (7.69%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Atrial fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	0	15	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 13 (7.69%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Balance disorder			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Facial paralysis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Epilepsy			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Dysgeusia			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Dizziness			
subjects affected / exposed	2 / 13 (15.38%)	36 / 206 (17.48%)	0 / 3 (0.00%)
occurrences (all)	2	52	0
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Head discomfort			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	8 / 13 (61.54%)	65 / 206 (31.55%)	0 / 3 (0.00%)
occurrences (all)	18	107	0
Hemiparesis			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0

Hydrocephalus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Facial paresis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Neuralgia			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Memory impairment			
subjects affected / exposed	3 / 13 (23.08%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	3	6	0
Intercostal neuralgia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
IIIrd nerve disorder			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Neuropathy peripheral			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Paraesthesia			
subjects affected / exposed	1 / 13 (7.69%)	17 / 206 (8.25%)	0 / 3 (0.00%)
occurrences (all)	1	17	0
Palatal palsy			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Nystagmus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	6	0

Polyneuropathy			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Pyramidal tract syndrome			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Sciatica			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
VIth nerve disorder			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	1	13	0
Anaemia			
subjects affected / exposed	4 / 13 (30.77%)	48 / 206 (23.30%)	0 / 3 (0.00%)
occurrences (all)	5	54	0
Lymphopenia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	4	5	0
Microcytic anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	1 / 13 (7.69%)	24 / 206 (11.65%)	1 / 3 (33.33%)
occurrences (all)	1	27	1
Thrombocytopenia			
subjects affected / exposed	1 / 13 (7.69%)	20 / 206 (9.71%)	0 / 3 (0.00%)
occurrences (all)	1	28	0
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Hypoacusis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Tinnitus			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Vertigo			
subjects affected / exposed	3 / 13 (23.08%)	11 / 206 (5.34%)	0 / 3 (0.00%)
occurrences (all)	4	15	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Cataract			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Diplopia			
subjects affected / exposed	2 / 13 (15.38%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Eye pain			
subjects affected / exposed	1 / 13 (7.69%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Eyelid oedema			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Iritis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Lacrimation increased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Vision blurred			

subjects affected / exposed	2 / 13 (15.38%)	23 / 206 (11.17%)	0 / 3 (0.00%)
occurrences (all)	2	33	0
Papilloedema			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Photophobia			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	1	6	0
Saccadic eye movement			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Uveitis			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	3	6	0
Macular oedema			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Visual impairment			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	1	14	0
Vitreous floaters			
subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Abdominal distension			
subjects affected / exposed	2 / 13 (15.38%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	2	7	0
Diarrhoea			
subjects affected / exposed	4 / 13 (30.77%)	53 / 206 (25.73%)	1 / 3 (33.33%)
occurrences (all)	11	89	1
Abdominal pain lower			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0

Abdominal pain upper			
subjects affected / exposed	2 / 13 (15.38%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	3	18	0
Constipation			
subjects affected / exposed	4 / 13 (30.77%)	56 / 206 (27.18%)	1 / 3 (33.33%)
occurrences (all)	4	64	1
Abdominal pain			
subjects affected / exposed	2 / 13 (15.38%)	26 / 206 (12.62%)	2 / 3 (66.67%)
occurrences (all)	3	31	3
Dry mouth			
subjects affected / exposed	2 / 13 (15.38%)	27 / 206 (13.11%)	0 / 3 (0.00%)
occurrences (all)	2	33	0
Dyspepsia			
subjects affected / exposed	3 / 13 (23.08%)	14 / 206 (6.80%)	0 / 3 (0.00%)
occurrences (all)	4	20	0
Dysphagia			
subjects affected / exposed	1 / 13 (7.69%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences (all)	1	8	0
Flatulence			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Noninfective gingivitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Gingival bleeding			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Haemorrhoids			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hyperaesthesia teeth			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	7 / 13 (53.85%)	84 / 206 (40.78%)	0 / 3 (0.00%)
occurrences (all)	18	130	0

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 13 (7.69%)	16 / 206 (7.77%)	1 / 3 (33.33%)
occurrences (all)	4	20	1
Oral pain			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Retching			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Salivary gland mass			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Stomatitis			
subjects affected / exposed	2 / 13 (15.38%)	12 / 206 (5.83%)	0 / 3 (0.00%)
occurrences (all)	2	17	0
Vomiting			
subjects affected / exposed	4 / 13 (30.77%)	55 / 206 (26.70%)	1 / 3 (33.33%)
occurrences (all)	6	89	1
Toothache			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	1	6	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 13 (0.00%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Dry skin			
subjects affected / exposed	5 / 13 (38.46%)	33 / 206 (16.02%)	1 / 3 (33.33%)
occurrences (all)	6	38	1
Dermatitis acneiform			
subjects affected / exposed	2 / 13 (15.38%)	34 / 206 (16.50%)	0 / 3 (0.00%)
occurrences (all)	2	53	0
Alopecia			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	1	12	0
Actinic keratosis			

subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Acne			
subjects affected / exposed	1 / 13 (7.69%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Erythema			
subjects affected / exposed	3 / 13 (23.08%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	12	27	0
Erythema nodosum			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	2	7	0
Hyperkeratosis			
subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Hyperhidrosis			
subjects affected / exposed	0 / 13 (0.00%)	9 / 206 (4.37%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Hidradenitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	4	4	0
Ingrowing nail			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Piloerection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Night sweats			
subjects affected / exposed	3 / 13 (23.08%)	13 / 206 (6.31%)	2 / 3 (66.67%)
occurrences (all)	3	16	2
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Papule			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	1 / 3 (33.33%)
occurrences (all)	0	3	1

Photosensitivity reaction			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Nail discolouration			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Rash maculo-papular			
subjects affected / exposed	1 / 13 (7.69%)	28 / 206 (13.59%)	1 / 3 (33.33%)
occurrences (all)	2	69	1
Rash			
subjects affected / exposed	4 / 13 (30.77%)	52 / 206 (25.24%)	0 / 3 (0.00%)
occurrences (all)	11	80	0
Pruritus			
subjects affected / exposed	6 / 13 (46.15%)	25 / 206 (12.14%)	0 / 3 (0.00%)
occurrences (all)	6	31	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Skin striae			
subjects affected / exposed	2 / 13 (15.38%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Skin plaque			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Skin mass			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	3	8	0
Skin lesion			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Skin atrophy			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

Xeroderma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Chromaturia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	1 / 13 (7.69%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	1	21	0
Pollakiuria			
subjects affected / exposed	0 / 13 (0.00%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Proteinuria			
subjects affected / exposed	3 / 13 (23.08%)	9 / 206 (4.37%)	0 / 3 (0.00%)
occurrences (all)	6	12	0
Renal failure			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Urinary retention			
subjects affected / exposed	2 / 13 (15.38%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	2	5	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	1 / 13 (7.69%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Joint stiffness			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0

Muscle spasms			
subjects affected / exposed	2 / 13 (15.38%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	4	20	0
Arthralgia			
subjects affected / exposed	7 / 13 (53.85%)	48 / 206 (23.30%)	0 / 3 (0.00%)
occurrences (all)	11	76	0
Arthritis			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Back pain			
subjects affected / exposed	3 / 13 (23.08%)	30 / 206 (14.56%)	0 / 3 (0.00%)
occurrences (all)	4	35	0
Bone pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Foot deformity			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Joint range of motion decreased			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Muscle twitching			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			
subjects affected / exposed	2 / 13 (15.38%)	30 / 206 (14.56%)	0 / 3 (0.00%)
occurrences (all)	2	41	0
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Neck mass			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	2	2	0

Pain in jaw			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Myalgia			
subjects affected / exposed	2 / 13 (15.38%)	45 / 206 (21.84%)	0 / 3 (0.00%)
occurrences (all)	2	96	0
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Muscular weakness			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	2	11	0
Myopathy			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Synovial cyst			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Spinal pain			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Abdominal abscess			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	3	3	0
Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	1	8	0
COVID-19			

subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	0	11	0
Folliculitis			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	4	16	0
Nasopharyngitis			
subjects affected / exposed	5 / 13 (38.46%)	20 / 206 (9.71%)	0 / 3 (0.00%)
occurrences (all)	15	37	0
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	2	6	0
Gingivitis			
subjects affected / exposed	2 / 13 (15.38%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Infection			
subjects affected / exposed	0 / 13 (0.00%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Fungal infection			
subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Onychomycosis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Oral candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Oral herpes			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Oropharyngeal candidiasis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 13 (7.69%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	1	11	0
Pharyngitis			
subjects affected / exposed	2 / 13 (15.38%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	9 / 206 (4.37%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Rash pustular			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	7 / 206 (3.40%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Paronychia			
subjects affected / exposed	1 / 13 (7.69%)	5 / 206 (2.43%)	0 / 3 (0.00%)
occurrences (all)	1	8	0
Skin candida			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Skin infection			
subjects affected / exposed	0 / 13 (0.00%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Streptococcal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Subcutaneous abscess			
subjects affected / exposed	1 / 13 (7.69%)	1 / 206 (0.49%)	0 / 3 (0.00%)
occurrences (all)	3	3	0
Tooth infection			
subjects affected / exposed	0 / 13 (0.00%)	10 / 206 (4.85%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Upper respiratory tract infection			

subjects affected / exposed	0 / 13 (0.00%)	21 / 206 (10.19%)	0 / 3 (0.00%)
occurrences (all)	0	28	0
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	22 / 206 (10.68%)	1 / 3 (33.33%)
occurrences (all)	1	31	1
Tooth abscess			
subjects affected / exposed	1 / 13 (7.69%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 206 (0.97%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Decreased appetite			
subjects affected / exposed	2 / 13 (15.38%)	40 / 206 (19.42%)	0 / 3 (0.00%)
occurrences (all)	2	49	0
Dehydration			
subjects affected / exposed	1 / 13 (7.69%)	4 / 206 (1.94%)	0 / 3 (0.00%)
occurrences (all)	2	5	0
Diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	3 / 206 (1.46%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypercalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Hyperglycaemia			
subjects affected / exposed	2 / 13 (15.38%)	44 / 206 (21.36%)	0 / 3 (0.00%)
occurrences (all)	2	74	0
Hyperkalaemia			
subjects affected / exposed	1 / 13 (7.69%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences (all)	1	11	0
Hyperuricaemia			
subjects affected / exposed	1 / 13 (7.69%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences (all)	5	12	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 13 (0.00%)	20 / 206 (9.71%)	0 / 3 (0.00%)
occurrences (all)	0	23	0

Hypocalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	8 / 206 (3.88%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Hypophosphataemia			
subjects affected / exposed	2 / 13 (15.38%)	20 / 206 (9.71%)	0 / 3 (0.00%)
occurrences (all)	9	31	0
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	0	23	0
Hypomagnesaemia			
subjects affected / exposed	2 / 13 (15.38%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	3	24	0
Hyponatraemia			
subjects affected / exposed	0 / 13 (0.00%)	15 / 206 (7.28%)	0 / 3 (0.00%)
occurrences (all)	0	24	0
Hypoglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	6 / 206 (2.91%)	0 / 3 (0.00%)
occurrences (all)	0	13	0

Non-serious adverse events	Hairy Cell Leukemia (HCL)	Multiple Myeloma (MM)	High Grade (WHO G3/G4) Glioma (HGG)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 55 (100.00%)	9 / 10 (90.00%)	42 / 45 (93.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	1	0	3
Seborrhoeic keratosis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	2	0	2
Melanocytic naevus			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Lipoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Fibroma			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Basal cell carcinoma			
subjects affected / exposed	13 / 55 (23.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	21	0	1
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	8 / 55 (14.55%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	9	0	0
Hypertension			
subjects affected / exposed	8 / 55 (14.55%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	11	1	3
Hot flush			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	1
Flushing			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	7	0	0
Varicose vein			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	29 / 55 (52.73%)	3 / 10 (30.00%)	19 / 45 (42.22%)
occurrences (all)	76	3	23
Asthenia			
subjects affected / exposed	3 / 55 (5.45%)	1 / 10 (10.00%)	4 / 45 (8.89%)
occurrences (all)	5	1	7
Chills			
subjects affected / exposed	30 / 55 (54.55%)	2 / 10 (20.00%)	5 / 45 (11.11%)
occurrences (all)	147	2	5
Feeling cold			

subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	2	1	2
Influenza like illness			
subjects affected / exposed	7 / 55 (12.73%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	10	0	1
Injection site reaction			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Oedema peripheral			
subjects affected / exposed	27 / 55 (49.09%)	2 / 10 (20.00%)	3 / 45 (6.67%)
occurrences (all)	44	2	3
Mucosal inflammation			
subjects affected / exposed	1 / 55 (1.82%)	2 / 10 (20.00%)	2 / 45 (4.44%)
occurrences (all)	1	2	2
Nodule			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	1
Oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	6 / 55 (10.91%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	19	0	0
Pain			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Peripheral swelling			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Pyrexia			

subjects affected / exposed	41 / 55 (74.55%)	3 / 10 (30.00%)	11 / 45 (24.44%)
occurrences (all)	183	5	30
Thirst			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Xerosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Sarcoidosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	3 / 55 (5.45%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	3	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	13 / 55 (23.64%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	18	1	3
Dysphonia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Hiccups			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	7 / 55 (12.73%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	9	0	2
Cough			

subjects affected / exposed	30 / 55 (54.55%)	1 / 10 (10.00%)	8 / 45 (17.78%)
occurrences (all)	57	1	10
Lung disorder			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	5	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	7 / 55 (12.73%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	9	0	0
Pneumonitis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Pleural effusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	11 / 55 (20.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	15	0	1
Nasal congestion			
subjects affected / exposed	20 / 55 (36.36%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	32	0	0
Productive cough			
subjects affected / exposed	9 / 55 (16.36%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	12	0	0
Wheezing			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Psychiatric disorders			

Depressed mood			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Confusional state			
subjects affected / exposed	3 / 55 (5.45%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	6	2	4
Anxiety			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	5	0	0
Agitation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	5 / 55 (9.09%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	5	0	1
Emotional disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	9 / 55 (16.36%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	9	1	2
Libido decreased			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Mood swings			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			

subjects affected / exposed	18 / 55 (32.73%)	0 / 10 (0.00%)	9 / 45 (20.00%)
occurrences (all)	39	0	9
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 55 (38.18%)	0 / 10 (0.00%)	9 / 45 (20.00%)
occurrences (all)	53	0	13
Blood alkaline phosphatase increased			
subjects affected / exposed	16 / 55 (29.09%)	2 / 10 (20.00%)	0 / 45 (0.00%)
occurrences (all)	29	2	0
Blood bilirubin increased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Blood creatinine increased			
subjects affected / exposed	13 / 55 (23.64%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	21	1	1
Blood glucose increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	4 / 55 (7.27%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	5	1	2
Blood oestrogen decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	7 / 55 (12.73%)	1 / 10 (10.00%)	5 / 45 (11.11%)
occurrences (all)	11	1	5
Blood urea increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			

subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	3	1	2
Blood testosterone decreased			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	5 / 55 (9.09%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	6	1	3
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	1	0	2
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	5	0	2
Neutrophil count decreased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	8 / 45 (17.78%)
occurrences (all)	5	0	25
Neutrophil count increased			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	1	0	3
Liver function test increased			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Urine output decreased			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0

Weight decreased			
subjects affected / exposed	3 / 55 (5.45%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	3	1	0
Weight increased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	2	0	1
White blood cell count decreased			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	6 / 45 (13.33%)
occurrences (all)	7	0	19
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	10 / 55 (18.18%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	11	0	0
Fall			
subjects affected / exposed	9 / 55 (16.36%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	11	0	1
Procedural pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Radiation associated pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Thermal burn			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Bradycardia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			

subjects affected / exposed	13 / 55 (23.64%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	15	0	2
Tachycardia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	7 / 55 (12.73%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	11	0	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences (all)	0	0	4
Balance disorder			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	1	0	2
Facial paralysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Epilepsy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	3 / 45 (6.67%)
occurrences (all)	0	0	7
Dysgeusia			
subjects affected / exposed	5 / 55 (9.09%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	7	0	0
Dizziness			
subjects affected / exposed	20 / 55 (36.36%)	1 / 10 (10.00%)	5 / 45 (11.11%)
occurrences (all)	35	1	6
Hypoaesthesia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 10 (10.00%)	3 / 45 (6.67%)
occurrences (all)	1	1	3
Head discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	21 / 55 (38.18%)	0 / 10 (0.00%)	18 / 45 (40.00%)
occurrences (all)	45	0	22

Hemiparesis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	3 / 45 (6.67%)
occurrences (all)	0	0	3
Hydrocephalus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Facial paresis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	5	0	0
Memory impairment			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	2	0	1
Intercostal neuralgia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
IIIrd nerve disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Peripheral motor neuropathy			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Paraesthesia			
subjects affected / exposed	9 / 55 (16.36%)	1 / 10 (10.00%)	4 / 45 (8.89%)
occurrences (all)	9	1	4
Palatal palsy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0

Peripheral sensory neuropathy			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	4	0	1
Polyneuropathy			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
VIth nerve disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	5	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences (all)	1	0	7
Anaemia			
subjects affected / exposed	10 / 55 (18.18%)	3 / 10 (30.00%)	9 / 45 (20.00%)
occurrences (all)	11	3	10
Lymphopenia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Microcytic anaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	6 / 55 (10.91%)	4 / 10 (40.00%)	7 / 45 (15.56%)
occurrences (all)	8	4	8
Thrombocytopenia			

subjects affected / exposed	3 / 55 (5.45%)	3 / 10 (30.00%)	4 / 45 (8.89%)
occurrences (all)	4	3	4
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	7 / 55 (12.73%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	7	0	0
Hypoacusis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Tinnitus			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Vertigo			
subjects affected / exposed	6 / 55 (10.91%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	9	0	2
Eye disorders			
Dry eye			
subjects affected / exposed	5 / 55 (9.09%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	5	1	0
Cataract			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Diplopia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	2	0	1
Eyelid oedema			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Iritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			

subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Vision blurred			
subjects affected / exposed	14 / 55 (25.45%)	0 / 10 (0.00%)	5 / 45 (11.11%)
occurrences (all)	24	0	5
Papilloedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	3 / 45 (6.67%)
occurrences (all)	1	0	3
Saccadic eye movement			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Macular oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	7	0	1
Vitreous floaters			
subjects affected / exposed	7 / 55 (12.73%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	7	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	2	1	0
Diarrhoea			
subjects affected / exposed	19 / 55 (34.55%)	3 / 10 (30.00%)	5 / 45 (11.11%)
occurrences (all)	36	3	7

Abdominal pain lower			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	1
Constipation			
subjects affected / exposed	22 / 55 (40.00%)	3 / 10 (30.00%)	8 / 45 (17.78%)
occurrences (all)	28	3	9
Abdominal pain			
subjects affected / exposed	12 / 55 (21.82%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	14	2	2
Dry mouth			
subjects affected / exposed	8 / 55 (14.55%)	1 / 10 (10.00%)	3 / 45 (6.67%)
occurrences (all)	12	1	3
Dyspepsia			
subjects affected / exposed	5 / 55 (9.09%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	6	0	1
Dysphagia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Noninfective gingivitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0

Nausea			
subjects affected / exposed	27 / 55 (49.09%)	5 / 10 (50.00%)	14 / 45 (31.11%)
occurrences (all)	45	6	16
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 55 (10.91%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	6	1	2
Oral pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Retching			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Salivary gland mass			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	1
Vomiting			
subjects affected / exposed	13 / 55 (23.64%)	3 / 10 (30.00%)	11 / 45 (24.44%)
occurrences (all)	18	7	13
Toothache			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	4	0	3
Dry skin			
subjects affected / exposed	17 / 55 (30.91%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	17	0	6
Dermatitis acneiform			
subjects affected / exposed	22 / 55 (40.00%)	0 / 10 (0.00%)	5 / 45 (11.11%)
occurrences (all)	35	0	7
Alopecia			

subjects affected / exposed	2 / 55 (3.64%)	2 / 10 (20.00%)	4 / 45 (8.89%)
occurrences (all)	2	2	4
Actinic keratosis			
subjects affected / exposed	6 / 55 (10.91%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	8	0	0
Acne			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	0	0	4
Erythema			
subjects affected / exposed	5 / 55 (9.09%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	8	0	1
Erythema nodosum			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Hyperkeratosis			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	5	0	1
Hyperhidrosis			
subjects affected / exposed	8 / 55 (14.55%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	11	0	1
Hidradenitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Piloerection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0

Papule			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Photosensitivity reaction			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	4	0	1
Nail discolouration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	19 / 55 (34.55%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	58	0	0
Rash			
subjects affected / exposed	11 / 55 (20.00%)	3 / 10 (30.00%)	12 / 45 (26.67%)
occurrences (all)	17	3	22
Pruritus			
subjects affected / exposed	10 / 55 (18.18%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	14	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Skin striae			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Skin plaque			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	2	1	0
Skin lesion			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0

Skin atrophy			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Xeroderma			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Chromaturia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	10 / 55 (18.18%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	14	0	2
Pollakiuria			
subjects affected / exposed	9 / 55 (16.36%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	9	0	0
Proteinuria			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	2	0	1
Renal failure			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1

Joint stiffness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	6 / 55 (10.91%)	0 / 10 (0.00%)	5 / 45 (11.11%)
occurrences (all)	7	0	7
Arthralgia			
subjects affected / exposed	21 / 55 (38.18%)	2 / 10 (20.00%)	7 / 45 (15.56%)
occurrences (all)	40	2	7
Arthritis			
subjects affected / exposed	5 / 55 (9.09%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	6	0	0
Back pain			
subjects affected / exposed	13 / 55 (23.64%)	1 / 10 (10.00%)	3 / 45 (6.67%)
occurrences (all)	15	1	4
Bone pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	3	1	0
Foot deformity			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Muscle twitching			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	19 / 55 (34.55%)	1 / 10 (10.00%)	4 / 45 (8.89%)
occurrences (all)	27	1	5
Neck pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	7	0	2

Neck mass			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	25 / 55 (45.45%)	1 / 10 (10.00%)	7 / 45 (15.56%)
occurrences (all)	71	1	11
Musculoskeletal pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Muscular weakness			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	4 / 45 (8.89%)
occurrences (all)	2	1	4
Myopathy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Spinal pain			
subjects affected / exposed	0 / 55 (0.00%)	2 / 10 (20.00%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Abdominal abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Bronchitis			

subjects affected / exposed	5 / 55 (9.09%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	7	0	0
COVID-19			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	8 / 55 (14.55%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	9	0	0
Folliculitis			
subjects affected / exposed	2 / 55 (3.64%)	1 / 10 (10.00%)	3 / 45 (6.67%)
occurrences (all)	3	1	5
Nasopharyngitis			
subjects affected / exposed	4 / 55 (7.27%)	1 / 10 (10.00%)	7 / 45 (15.56%)
occurrences (all)	7	1	11
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Gingivitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Infection			
subjects affected / exposed	2 / 55 (3.64%)	2 / 10 (20.00%)	1 / 45 (2.22%)
occurrences (all)	2	2	3
Fungal infection			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	4	0	2
Onychomycosis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Oral herpes			

subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	5	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	4 / 55 (7.27%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	5	1	1
Pharyngitis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Pneumonia			
subjects affected / exposed	6 / 55 (10.91%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	7	0	1
Rash pustular			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Rhinitis			
subjects affected / exposed	5 / 55 (9.09%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	6	1	0
Paronychia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	3 / 45 (6.67%)
occurrences (all)	0	0	6
Skin candida			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	5	0	0
Streptococcal infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Subcutaneous abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Tooth infection			

subjects affected / exposed	8 / 55 (14.55%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	11	0	0
Upper respiratory tract infection			
subjects affected / exposed	15 / 55 (27.27%)	0 / 10 (0.00%)	2 / 45 (4.44%)
occurrences (all)	20	0	3
Urinary tract infection			
subjects affected / exposed	8 / 55 (14.55%)	2 / 10 (20.00%)	6 / 45 (13.33%)
occurrences (all)	14	2	9
Tooth abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Decreased appetite			
subjects affected / exposed	7 / 55 (12.73%)	3 / 10 (30.00%)	6 / 45 (13.33%)
occurrences (all)	10	4	6
Dehydration			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Diabetes mellitus			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	25 / 55 (45.45%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences (all)	53	0	5
Hyperkalaemia			
subjects affected / exposed	4 / 55 (7.27%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	5	0	3
Hyperuricaemia			
subjects affected / exposed	3 / 55 (5.45%)	0 / 10 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0

Hypoalbuminaemia			
subjects affected / exposed	6 / 55 (10.91%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences (all)	6	0	4
Hypocalcaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 10 (10.00%)	2 / 45 (4.44%)
occurrences (all)	0	1	2
Hypophosphataemia			
subjects affected / exposed	11 / 55 (20.00%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences (all)	14	0	5
Hypokalaemia			
subjects affected / exposed	3 / 55 (5.45%)	2 / 10 (20.00%)	2 / 45 (4.44%)
occurrences (all)	6	3	2
Hypomagnesaemia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	4 / 45 (8.89%)
occurrences (all)	2	0	7
Hyponatraemia			
subjects affected / exposed	2 / 55 (3.64%)	0 / 10 (0.00%)	1 / 45 (2.22%)
occurrences (all)	3	0	2
Hypoglycaemia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 10 (0.00%)	3 / 45 (6.67%)
occurrences (all)	5	0	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2013	Amendment 1: • Added EudraCT Number. • Removed cardiac enzyme (troponin) from list of clinical laboratory assessments to be completed. • Clarified inclusion criteria. Mandatory tumor sample and BM aspirate sample are required at Screening. • Added text to the exclusion criteria to confirm that no histology-specific exclusion criteria were included. • Corrected reference to CT scan (i.e., changed to MRI scan) as CT is not permitted in these cohorts. • Removed statement that progressive disease sample collection was mandatory for ATC, HCL and MM cohorts as it was inconsistent with the time and events tables.
18 December 2013	Amendment 2: •Primary endpoint: added use of Modified RANO and RANO response criteria in gliomas •Inclusion criteria: deleted reference to CLIA approved laboratory; revised prior treatment for subjects with MM; added: GIST subjects require progression on imatinib and sunitinib; Added subjects with specified histology and no available treatment options per local or regional SOC; Added for WHO Grade 2 glioma: only subjects not suitable for chemotherapy eligible •Safety: Added estimation of blood volume collected during study; Removed reference to QTcF as stopping criteria for QTc prolongation is limited to use of Bazett formula for correction; Removed use of MUGA scan to assess cardiac ejection fraction; added procedure to be performed by same operator throughout the study; removed requirement of reporting symptomatic events as SAE, and in case of asymptomatic absolute decrease of >10% in LVEF compared to baseline and ejection fraction below institutional LLN, study treatment must be discontinued; Added "Monitoring of Non-Cutaneous Secondary/Recurrent Malignancy" for use of dabrafenib; Revised: CV events may occur also with dabrafenib or in combination and revised QTc prolongation; Clarified management of hypertension with persistent increase in systolic and/or diastolic BP to be managed by recommendations and study treatment to discontinue in asymptomatic or symptomatic hypertension; Revised cutaneous SCC to remove reference to keratoacanthomas; added requirement of dermatological examinations monthly for 6 months after treatment discontinuation; "Medications to be Used with Caution": updated reference for drugs known to induce QTc prolongation; inclusion of guidelines for management and dose reduction for renal insufficiency when considered treatment related; Added new section: Formation of data monitoring committee to review safety and efficacy data during interim analyses and to indicate that independent hematologist and oncologist will serve on this committee.
21 July 2014	Amendment 3: • Revised dabrafenib and trametinib sections in the protocol to delete redundant information, updated with revised protocol language and standard asset language. • Revised the "Concomitant medication and non-drug therapies section" to clarify the use of anticoagulants, palliative radiation and use of dabrafenib during radiotherapy. • Added language pertaining to retrospective confirmation of histology type for ATC cohort. • Revised the vision changes and ophthalmic exam language with standard asset language. • Revised the disease assessment sections to clarify type of assessment, timing and evaluation criteria. • Revised the stopping criteria, management, and dose modification for special events to reflect changes in standard asset language. Added Ex Vivo sub study for HCL cohort.

24 October 2014	Amendment 4: • Revised the protocol in response to the recent decision for the substantial amendment of a Voluntary Harmonization Procedure (VHP-SA) submission of Amendment 3 of the protocol. • Revised to update regulatory approval status of trametinib monotherapy and trametinib in combination with dabrafenib. • Revised Inclusion criteria #5 and #4, respectively, to clarify that the criterion applies to subjects who are already receiving corticosteroid therapy. • Revised to criterion #1 to clarify that the status of delayed toxicity applies to all types of therapy and not solely chemotherapy. • Revised text to align with the Summary of Product Characteristics language as requested by the VHP.
28 April 2015	Amendment 5: • Revised LVEF stopping criteria to indicate when to report as SAE. • Removed BRAT diet from diarrhea management guidelines. • Removed oral contraceptives from the prohibited medications list and provided supporting information regarding interaction with dabrafenib. • Specified oral formulation for selected prohibited medications and medications to be used with caution. • Clarified which samples to be submitted for confirmation of BRAF mutation status; definition of SAEs revised for protocol specific SAEs based on updated list of AE of special interest. • Removed ATC sample collection for possible independent histology confirmation. • Added new section for malignancies to include section on cutaneous squamous cell carcinoma, new primary melanoma and non-cutaneous malignancies based on updated asset language for dabrafenib and trametinib. • Clarified use of NSAIDs in subjects with MM for pyrexia and action to be taken with dabrafenib with pneumonitis. • Revised disease assessments for solid tumors to clarify imaging modality to be used for specific cohorts. • Revised the statistical section to reflect change in study sample size and trial simulation output.
05 January 2016	Amendment 6: • Updated the risk assessment for dabrafenib and trametinib combination therapy. • Clarified the dose modification wording for dabrafenib and trametinib with respect to drug reductions and re-escalation. • Re-implemented ATC pathology sample collection for a potential independent histology confirmation. It also implemented samples collection for a potential independent histology confirmation for WHO Grade 1-4 Glioma cohorts. • Clarified the disease assessment method for WHO Grade 1-4 Glioma cohort. • Updated the baseline and on-treatment assessments for the HCL cohort. • Added additional analysis populations that are planned for the interim analyses. • Added expansion cohorts for all cohorts that meet the criteria for early stopping for efficacy at an interim analysis. • Clarified the definition for DOR for all response categories.
19 July 2016	Amendment 7: • Deleted/replaced references to GlaxoSmithKline or its staff with that of Novartis and its authorized agents to align with the change of sponsorship. • Made administrative changes to align with Novartis processes and procedures.

14 December 2017	Amendment 8: • Updated Time and Event table for pregnancy, blood sample for CBC, peripheral blood sample staining for hairy cell count, flow cytometry for peripheral blood sample, and extended follow-ups to align with the footnotes. Added TSH, free T4 for ATC cohort only. Modified the instruction for HCL subjects who were tolerating study drug treatment beyond week 48. These subjects could reduce the frequency of response assessment evaluation from every 4 weeks (+/- 3 days) to every 8 weeks (+/-3 days) if appropriate in the judgement of the treating investigator. • Evaluations at extended follow up were updated. • Updated post-baseline Laboratory and Disease Assessments for HCL subjects. • Clarified HbA1c testing is included in "Clinical Chemistry. • Updated the contraception requirements for male subjects. • Updated medications to be used with Caution: removed statement regarding Dabrafenib solubility at higher pH. Consequently, proton pump inhibitors removed from Medications to be used with Caution. • Reinstated a sentence outlining the time period for detecting adverse events and serious adverse events inadvertently removed at amendment 7. • Corrected the number of samples and amount of peripheral blood to be collected. • Updated RANO Response Criteria under 'Disease progression (PD) for WHO Grade 1 or 2 Glioma.
12 February 2019	Amendment 9: • Updated change to contraception requirements for female subjects. • Updated definition for study completion and updated language clarifying the possible options for alternative supply of study treatment for those subjects who continue to derive clinical benefit at study completion. • Clarified the analysis population for supportive final efficacy analysis. • Updated date of final analyses as the date representing a minimum follow up of approximately 2 years for all subjects enrolled. • Removed reference to pooled ORR calculations across histologies.
09 January 2020	Amendment 10: • The primary purpose of amendment 10 is to align the dose modification section of the protocol related to severe cutaneous adverse reactions, as updated in the dabrafenib and trametinib investigator's brochures edition 11. • In addition, baseline results of IDH mutation status and MGMT methylation status were to be collected as part of disease characteristics for subjects in the LGG or HGG cohorts only. Data collected only where available as part of medical records; retrospective testing is not requested or required. • References to the use of oral (hormonal) contraceptives being "permitted" or "used with caution" were removed from the relevant sections in alignment with changes made at protocol amendment #9 to update female contraception requirements. These sections were inadvertently not updated at the previous amendment.
04 June 2020	Amendment 11: • The main purposes of this amendment were to extend the study by one additional year for more mature estimates of duration of response, progression free survival and overall survival; and to change the primary analysis population of the final efficacy analysis from the BRAF V600E population to the ITT population. • To reduce burden on subjects, collections for blood and tissue samples for predictive and pharmacodynamic biomarker research as well as PK sampling at follow up were discontinued as the majority of the planned biomarker analyses have been completed and the PK profile of the regimen is now well characterized. • Disease assessment intervals after the first 48 weeks of study treatment for subjects in the HCL cohort was extended from "at least every 8 weeks" to "at least every 12 weeks".

Notes:

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com for complete trial results.

Notes: