Clinical trial results:
A phase II, multicenter study of oral cMET inhibitor INC280 in adult patients with EGFR wild-type (wt), advanced non-small cell lung cancer (NSCLC)

Summary

EudraCT number	2014-003850-15
Trial protocol	AT DE ES NL FR BE SE GB IT
Global end of trial date	16 May 2023

Results information

Result version number	v1 (current)
This version publication date	07 March 2024
First version publication date	07 March 2024

Trial information

Trial identification

Sponsor protocol code	CINC280A2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02414139
WHO universal trial number (UTN)	-

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	16 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the antitumor activity of capmatinib, as measured by overall response rate (ORR) by Blinded Independent Review Committee (BIRC) assessment, by cohort.

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	11 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Austria: 15
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 64
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Japan: 46
Country: Number of subjects enrolled	Korea, Republic of: 21
Country: Number of subjects enrolled	Lebanon: 4
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Netherlands: 26
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Singapore: 7
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United Kingdom: 4

Country: Number of subjects enrolled	United States: 42
Worldwide total number of subjects	373
EEA total number of subjects	218

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)	147
From 65 to 84 years	217
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in 95 centers across 20 countries

Pre-assignment

Screening details:

Screening assessments were conducted up to 28 days prior to the start of study treatment

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1a: 2/3L, MET GCN ≥ 10

Arm description:

Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 1a, capmatinib was administered in a fasted state.

Arm title	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10

Arm description:

Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 1b, capmatinib was administered in a fasted state.

Arm title	Cohort 2: 2/3L, 4 ≤ MET GCN < 6

Arm description:

Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)

Arm type	Experimental

Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 2, capmatinib was administered in a fasted state.

Arm title	Cohort 3: 2/3L, MET GCN < 4

Arm description:

Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 3, capmatinib was administered in a fasted state.

Arm title	Cohort 4: 2/3L, Mutant

Arm description:

Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 4, capmatinib was administered in a fasted state.

Arm title	Cohort 5a: 1L, MET GCN ≥10

Arm description:

Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 5a, capmatinib was administered in a fasted state.

Arm title	Cohort 5b: 1L, Mutant

Arm description:

Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)

Arm type	Experimental

Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 5b, capmatinib was administered in a fasted state.

Arm title	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10

Arm description:

Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 6, capmatinib was administered either with or without food.

Arm title	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant

Arm description:

Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 6, capmatinib was administered either with or without food.

Arm title	Cohort 7 (expansion of Cohort 5b): 1L, Mutant

Arm description:

Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib was administered orally, at a dose of 400 mg on a continuous twice daily dosing schedule. For participants in Cohort 7, capmatinib was administered either with or without food.

Number of subjects in period 1	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6
Started	69	42	54
Completed	0	0	0
Not completed	69	42	54
Adverse event, serious fatal	-	-	1
Physician decision	5	4	6
Adverse event, non-fatal	11	6	8
Protocol deviation	-	-	1
Subject/Guardian decision	5	1	1
Study terminated (as per protocol) by Sponsor	-	-	-
Progressive disease	48	31	37

Number of subjects in period 1	Cohort 3: 2/3L, MET GCN < 4	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10
Started	30	69	15
Completed	0	0	0
Not completed	30	69	15
Adverse event, serious fatal	1	-	-
Physician decision	1	4	-
Adverse event, non-fatal	5	14	3
Protocol deviation	-	-	-
Subject/Guardian decision	2	5	-
Study terminated (as per protocol) by Sponsor	-	3	-
Progressive disease	21	43	12

Number of subjects in period 1	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant
Started	28	3	31
Completed	0	0	0
Not completed	28	3	31
Adverse event, serious fatal	-	-	-
Physician decision	2	-	1
Adverse event, non-fatal	6	1	6
Protocol deviation	-	-	-
Subject/Guardian decision	2	-	1
Study terminated (as per protocol) by Sponsor	2	-	3
Progressive disease	16	2	20

Number of subjects in period 1	Cohort 7 (expansion of Cohort 5b): 1L, Mutant
Started	32

Completed	0
Not completed	32
Adverse event, serious fatal	1
Physician decision	4
Adverse event, non-fatal	8
Protocol deviation	-
Subject/Guardian decision	1
Study terminated (as per protocol) by Sponsor	4
Progressive disease	14

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1a: 2/3L, MET GCN ≥ 10
Reporting group description:	
Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10
Reporting group description:	
Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	
Reporting group title	Cohort 2: 2/3L, 4 ≤ MET GCN < 6
Reporting group description:	
Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 3: 2/3L, MET GCN < 4
Reporting group description:	
Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 4: 2/3L, Mutant
Reporting group description:	
Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 5a: 1L, MET GCN ≥10
Reporting group description:	
Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	
Reporting group title	Cohort 5b: 1L, Mutant
Reporting group description:	
Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	
Reporting group title	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Reporting group description:	
Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	
Reporting group title	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant
Reporting group description:	
Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	
Reporting group title	Cohort 7 (expansion of Cohort 5b): 1L, Mutant
Reporting group description:	
Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	

Reporting group values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6
Number of subjects	69	42	54
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)	41	29	30
From 65-84 years	28	13	24
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	60.9	59.5	61.7
standard deviation	± 9.56	± 9.11	± 10.00
Sex: Female, Male			
Units: Participants			
Female	15	21	15
Male	54	21	39
Race/Ethnicity, Customized			
Units: Subjects			
Asian	17	4	14
Black	1	0	0
Caucasian	51	38	40
Native American	0	0	0
Unknown	0	0	0
Other	0	0	0

Reporting group values	Cohort 3: 2/3L, MET GCN < 4	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10
Number of subjects	30	69	15
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)	16	14	5
From 65-84 years	14	51	8
85 years and over	0	4	2
Age Continuous			
Units: Years			
arithmetic mean	61.7	71.0	68.2
standard deviation	± 9.23	± 8.32	± 10.36
Sex: Female, Male			
Units: Participants			
Female	11	40	4
Male	19	29	11
Race/Ethnicity, Customized			
Units: Subjects			
Asian	11	19	6
Black	0	0	0
Caucasian	19	49	9
Native American	0	1	0
Unknown	0	0	0

Other	0	0	0

Reporting group values	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant
Number of subjects	28	3	31
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)	3	2	4
From 65-84 years	24	1	27
85 years and over	1	0	0
Age Continuous Units: Years			
arithmetic mean	72.4	60.7	69.0
standard deviation	± 7.02	± 10.69	± 6.29
Sex: Female, Male Units: Participants			
Female	18	1	16
Male	10	2	15
Race/Ethnicity, Customized Units: Subjects			
Asian	4	1	5
Black	0	0	1
Caucasian	24	1	24
Native American	0	0	1
Unknown	0	1	0
Other	0	0	0

Reporting group values	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Total	
Number of subjects	32	373	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	147	
From 65-84 years	27	217	

85 years and over	2	9	

Age Continuous Units: Years			
arithmetic mean	73.3		
standard deviation	± 8.35	-	
Sex: Female, Male Units: Participants			
Female	23	164	
Male	9	209	
Race/Ethnicity, Customized Units: Subjects			
Asian	3	84	
Black	1	3	
Caucasian	26	281	
Native American	0	2	
Unknown	0	1	
Other	2	2	

End points

End points reporting groups

Reporting group title	Cohort 1a: 2/3L, MET GCN ≥ 10
Reporting group description:	
Pre-treated patients with MET GCN ≥ 10 treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10
Reporting group description:	
Pre-treated patients with MET GCN ≥ 6 and < 10 treated with INC280 at 400 mg BID as second or third line (2/3L)	
Reporting group title	Cohort 2: 2/3L, 4 ≤ MET GCN < 6
Reporting group description:	
Pre-treated patients with MET GCN ≥ 4 and < 6 treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 3: 2/3L, MET GCN < 4
Reporting group description:	
Pre-treated patients with MET GCN < 4 treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 4: 2/3L, Mutant
Reporting group description:	
Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L)	
Reporting group title	Cohort 5a: 1L, MET GCN ≥10
Reporting group description:	
Treatment-naïve patients with MET GCN ≥10 treated with INC280 at 400mg BID as first-line (1L)	
Reporting group title	Cohort 5b: 1L, Mutant
Reporting group description:	
Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L)	
Reporting group title	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Reporting group description:	
Pre-treated patients with MET GCN ≥ 10 without MET mutation treated with INC280 at 400 mg BID as second line (2L) (expansion cohort of Cohort 1a)	
Reporting group title	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant
Reporting group description:	
Pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as second line (2L)(expansion of Cohort 4)	
Reporting group title	Cohort 7 (expansion of Cohort 5b): 1L, Mutant
Reporting group description:	
Treatment-naïve patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as first line (1L) (expansion cohort of Cohort 5b)	
Subject analysis set title	Cohort 4 + Cohort 6.2: 2/3L, Mutant
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All pre-treated patients with MET mutation regardless of MET GCN treated with INC280 at 400mg BID as second or third line (2/3L). (Participants from Cohort 4 and Cohort 6.2)	
Subject analysis set title	Cohort 5b + Cohort 7: 1L, Mutant
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All treatment naive patients with MET mutation regardless of MET GCN treated with INC280 at 400 mg BID as first line (1L) (Participants from Cohort 5b and Cohort 7)	
Subject analysis set title	Cohorts 1-5: Capmatinib administered in fasted state (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state and provided at least one evaluable PK concentration (for capmatinib or metabolite CMN288) (PK analysis set or PAS)

Subject analysis set title	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b who received capmatinib in fasted state and had an extensive PK collection schedule and provided at least one evaluable PK profile (for INC280 or metabolite CMN288) (Full PK analysis set or Full PAS)

Subject analysis set title	Cohorts 6-7: Capmatinib administered with/without food (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants from Cohorts 6 and 7 who received capmatinib with or without food and provided at least one evaluable PK concentration (for capmatinib or metabolite CMN288) (PK analysis set or PAS)

Subject analysis set title	All participants
Subject analysis set type	Full analysis

Subject analysis set description:

All participants

Primary: Overall Response Rate (ORR) by Blinded Independent Review Committee (BIRC) assessment

End point title	Overall Response Rate (ORR) by Blinded Independent Review Committee (BIRC) assessment[1]

End point description:

Percentage of participants with a best overall response defined as confirmed complete response (CR) or partial response (PR) by BIRC assessment per RECIST 1.1.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Primary

End point timeframe:

Up to approximately 5 years

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: No statistical analyses were planned for this endpoint

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	42	54	30
Units: Percentage of Participants				
number (confidence interval 95%)	29.0 (18.7 to 41.2)	11.9 (4.0 to 25.6)	9.3 (3.1 to 20.3)	6.7 (0.8 to 22.1)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	15	28	3
Units: Percentage of Participants				

number (confidence interval 95%)	40.6 (28.9 to 53.1)	40.0 (16.3 to 67.7)	67.9 (47.6 to 84.1)	0.0 (0.0 to 70.8)

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	100	60
Units: Percentage of Participants				
number (confidence interval 95%)	51.6 (33.1 to 69.8)	68.8 (50.0 to 83.9)	44.0 (34.1 to 54.3)	68.3 (55.0 to 79.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by BIRC assessment

End point title	Duration of Response (DOR) by BIRC assessment

End point description:

Time from the date of the first documented CR or PR by BIRC per RECIST 1.1 to the first documented progression or date of death due to any cause for patients with confirmed PR or CR. The Kaplan-Meier method was used to estimate DOR, and the median DOR, along with 95% confidence intervals was reported. If a subject did not have an event, DOR was censored at the date of last adequate tumor assessment.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
9999= not estimable

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	5	5	2
Units: Months				
median (confidence interval 95%)	8.31 (4.17 to 15.44)	24.94 (2.69 to 24.94)	9.66 (4.17 to 9999)	4.19 (4.17 to 4.21)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	6	19	0[2]
Units: Months				
median (confidence interval 95%)	9.72 (5.55 to 12.98)	7.54 (2.56 to 14.26)	12.58 (5.55 to 38.67)	(to)

Notes:

[2] - No participants had confirmed PR or CR

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	16	22	44	41
Units: Months				
median (confidence interval 95%)	9.05 (4.17 to 27.60)	16.59 (8.34 to 9999)	9.72 (5.62 to 12.98)	16.59 (8.41 to 22.11)

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by investigator assessment

End point title	ORR by investigator assessment

End point description:

Percentage of patients with a best overall response defined as confirmed CR or PR per RECIST 1.1 by investigator assessment.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	42	54	30
Units: Percentage of participants				
number (confidence interval 95%)	27.5 (17.5 to 39.6)	7.1 (1.5 to 19.5)	9.3 (3.1 to 20.3)	3.3 (0.1 to 17.2)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	15	28	3
Units: Percentage of participants				
number (confidence interval 95%)	43.5 (31.6 to 56.0)	40.0 (16.3 to 67.7)	60.7 (40.6 to 78.5)	0.0 (0.0 to 70.8)

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	100	60
Units: Percentage of participants				
number (confidence interval 95%)	45.2 (27.3 to 64.0)	56.3 (37.7 to 73.6)	44.0 (34.1 to 54.3)	58.3 (44.9 to 70.9)

Statistical analyses

No statistical analyses for this end point

Secondary: DOR by investigator assessment

End point title	DOR by investigator assessment

End point description:

Time from the date of the first documented CR or PR per RECIST 1.1 by investigator assessment to the first documented progression or death due to any cause for patients with confirmed PR or CR. The Kaplan-Meier method was used to estimate DOR, and the median DOR, along with 95% confidence intervals was reported. If a subject did not have an event, DOR was censored at the date of last adequate tumor assessment.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
9999= not estimable

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	3	5	1
Units: Months				
median (confidence interval 95%)	6.80 (4.21 to 20.73)	6.93 (5.75 to 8.34)	19.48 (2.83 to 9999)	6.93 (-9999 to 9999)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	6	17	0[3]
Units: Months				
median (confidence interval 95%)	8.31 (4.34 to 12.06)	9.66 (4.01 to 17.08)	13.83 (4.27 to 25.33)	(to)

Notes:

[3] - No participants had confirmed PR or CR

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	18	44	35
Units: Months				
median (confidence interval 95%)	14.57 (4.17 to 27.60)	15.21 (6.77 to 31.77)	8.38 (5.55 to 13.80)	13.96 (9.33 to 22.18)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) by BIRC assessment

End point title	Time to Response (TTR) by BIRC assessment

End point description:

Time between date of start of treatment until first documented response (confirmed CR or PR) per RECIST 1.1 by BIRC assessment.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	5	5	2
Units: Months				
median (full range (min-max))	1.4 (0.5 to 6.8)	2.8 (1.4 to 16.6)	1.4 (1.2 to 6.2)	3.4 (1.3 to 5.5)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	6	19	0[4]
Units: Months				
median (full range (min-max))	1.4 (1.2 to 5.6)	1.4 (1.2 to 2.9)	1.4 (1.3 to 6.9)	(to)

Notes:

[4] - No participant had confirmed PR or CR

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	16	22	44	41
Units: Months				
median (full range (min-max))	1.4 (1.1 to 9.8)	1.4 (1.2 to 7.2)	1.4 (1.1 to 9.8)	1.4 (1.2 to 7.2)

Statistical analyses

No statistical analyses for this end point

Secondary: TTR by investigator assessment

End point title	TTR by investigator assessment

End point description:

Time between date of start of treatment until first documented response (confirmed CR or PR) per RECIST 1.1 by investigator assessment.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	3	5	1
Units: Months				
median (full range (min-max))	1.4 (1.2 to 5.4)	1.4 (1.3 to 1.4)	1.3 (1.2 to 1.7)	1.3 (1.3 to 1.3)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of

				Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	6	17	0[5]
Units: Months				
median (full range (min-max))	1.4 (1.2 to 11.1)	1.4 (1.3 to 2.5)	1.4 (1.2 to 4.0)	(to)

Notes:

[5] - No participants had confirmed PR or CR

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	18	44	35
Units: Months				
median (full range (min-max))	1.4 (1.1 to 12.3)	1.4 (1.2 to 5.6)	1.4 (1.1 to 12.3)	1.4 (1.2 to 5.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

Percentage of participants with a best overall response of confirmed CR, PR or stable disease (SD) per RECIST 1.1 by BIRC and investigator assessment.
CR: Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target and non-target lesions must have a reduction in short axis to < 10 mm.
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	42	54	30
Units: Percentage of participants				
number (confidence interval 95%)				
By BIRC assessment	71.0 (58.8 to 81.3)	54.8 (38.7 to 70.2)	46.3 (32.6 to 60.4)	53.3 (34.3 to 71.7)
By investigator assessment	60.9 (48.4 to 72.4)	45.2 (29.8 to 61.3)	44.4 (30.9 to 58.6)	46.7 (28.3 to 65.7)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	15	28	3
Units: Percentage of participants				
number (confidence interval 95%)				
By BIRC assessment	78.3 (66.7 to 87.3)	66.7 (38.4 to 88.2)	96.4 (81.7 to 99.9)	100.0 (29.2 to 100.0)
By investigator assessment	76.8 (65.1 to 86.1)	73.3 (44.9 to 92.2)	96.4 (81.7 to 99.9)	100.0 (29.2 to 100.0)

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	100	60
Units: Percentage of participants				
number (confidence interval 95%)				
By BIRC assessment	90.3 (74.2 to 98.0)	100.0 (89.1 to 100.0)	82.0 (73.1 to 89.0)	98.3 (91.1 to 100.0)
By investigator assessment	90.3 (74.2 to 98.0)	96.9 (83.8 to 99.9)	81.0 (71.9 to 88.2)	96.7 (88.5 to 99.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Time from start of treatment to the date of the first documented progression or death due to any cause per RECIST 1.1 both by BIRC and investigator assessment. Clinical deterioration was not considered as a qualifying event for progression. PFS was censored at the last adequate tumor assessment if one of the following occurred: absence of event or the event occurred after two or more missing tumor assessments.
The Kaplan-Meier method was used to estimate PFS, and the median PFS, along with 95% confidence intervals, was reported.
Progressive disease: For target lesions, at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm^2. For non-target lesions, unequivocal progression of existing non-target lesions

End point type	Secondary

End point timeframe:

Up to approximately 5 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	42	54	30
Units: Months				
median (confidence interval 95%)				
By BIRC assessment	4.07 (2.86 to 4.83)	2.66 (1.41 to 3.09)	2.66 (1.41 to 4.14)	3.55 (2.20 to 4.21)
By investigator assessment	4.14 (2.79 to 5.52)	2.40 (1.45 to 2.83)	2.60 (1.48 to 3.09)	2.73 (1.45 to 3.78)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	15	28	3
Units: Months				
median (confidence interval 95%)				
By BIRC assessment	5.42 (4.17 to 6.97)	4.17 (1.45 to 6.87)	12.42 (8.21 to 23.39)	2.79 (2.07 to 4.24)
By investigator assessment	4.80 (4.11 to 7.75)	2.76 (1.45 to 6.87)	11.99 (5.52 to 16.92)	2.76 (2.07 to 2.79)

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	100	60
Units: Months				
median (confidence interval 95%)				
By BIRC assessment	6.93 (4.17 to 13.34)	12.45 (6.87 to 22.05)	5.49 (4.17 to 8.11)	12.45 (8.31 to 17.97)
By investigator assessment	6.90 (5.55 to 17.31)	9.79 (5.75 to 16.36)	6.60 (4.70 to 8.18)	11.07 (6.87 to 15.18)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Time from start of treatment to the date of death due to any cause. If the patient was alive at the date of the analysis cut-off or lost to follow-up, then OS was censored at the last contact date prior to data cut-off date.
The Kaplan-Meier method was used to estimate OS, and the median OS, along with 95% confidence intervals, was reported.
9999= not estimable

End point type	Secondary

End point timeframe:

Up to approximately 6 years

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	42	54	30
Units: Months				
median (confidence interval 95%)	10.61 (6.28 to 17.22)	7.46 (5.59 to 10.18)	10.15 (5.52 to 15.74)	9.46 (4.11 to 12.32)

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	15	28	3
Units: Months				
median (confidence interval 95%)	13.57 (8.61 to 22.24)	9.56 (4.80 to 9999)	20.76 (12.42 to 43.93)	4.14 (2.07 to 9999)

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	100	60
Units: Months				
median (confidence interval 95%)	25.95 (13.54 to 43.40)	21.36 (12.85 to 34.76)	16.79 (11.63 to 23.82)	21.36 (15.24 to 30.52)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) concentrations of capmatinib

End point title	Pharmacokinetic (PK) concentrations of capmatinib

End point description:

PK concentrations of capmatinib. Plasma concentrations of capmatinib were measured using validated liquid chromatography-tandem mass spectrometry (LCMS/MS) methods with a lower limit of quantification (LLOQ) of approximately 1.0 ng/mL.
Capmatinib concentration data was summarized for Cohorts 1a, 1b, 2, 3, 4, 5a and 5b when capmatinib was administered in fasted state; and for Cohorts 6 and 7 when capmatinib was administered with or without food.

End point type	Secondary

End point timeframe:

Cycle (C) 1 Day (D) 1 predose and 2 hours post-dose, C1D15 pre-dose and 2 hours post-dose, C3D1 pre-dose. Each Cycle is 21 days

End point values	Cohorts 1-5: Capmatinib administered in fasted state (PAS)	Cohorts 6-7: Capmatinib administered with/without food (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	275	54		
Units: nanogram/mililiter (ng/ml)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1- pre-dose (n= 275 / 54)	0.00 (± 0.00)	0.00 (± 0.00)		
Cycle 1 Day 1- 2 hours post-dose (n= 275 / 53)	3360 (± 1920)	3060 (± 1780)		
Cycle 1 Day 15 - pre-dose (n= 176 / 29)	727 (± 781)	663 (± 806)		
Cycle 1 Day 15- 2 hours post-dose (n= 209 / 47)	4100 (± 2100)	4340 (± 2000)		
Cycle 3 Day 1 - pre-dose (n= 96 / 18)	687 (± 1000)	672 (± 745)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of CMN288

End point title	Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of CMN288

End point description:

AUCinf of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. AUCinf is the area under the plasma concentration-time curve extrapolated to infinity. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng*h/ml				
arithmetic mean (standard deviation)				
Cycle 1 Day 1	9020 (± 5060)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration (Cmax) of CMN288

End point title	Maximum concentration (Cmax) of CMN288

End point description:

Cmax of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. Cmax is the maximum plasma drug concentration after single dose administration. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	51			
Units: ng/ml				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 51) Cycle 1 Day 15 (n= 42)	1910 (± 1420) 1420 (± 725)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration (Cmax) of capmatinib

End point title	Maximum concentration (Cmax) of capmatinib

End point description:

Cmax of capmatinib was estimated by non-compartmental analysis. Cmax is the maximum plasma drug concentration after single dose administration. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	55			
Units: ng/ml				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=55)	4230 (± 2290)			
Cycle 1 Day 15 (n=44)	5450 (± 2560)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of capmatinib

End point title	Area under the plasma concentration-time curve from zero to time infinity (AUCinf) of capmatinib

End point description:

AUCinf of capmatinib was estimated by non-compartmental analysis. AUCinf is the area under the plasma concentration-time curve extrapolated to infinity. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: nanogram * hour / mililiter (ng*h/ml)				

arithmetic mean (standard deviation)	17000 (± 7770)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum concentration (Tmax) of capmatinib

End point title	Time to reach maximum concentration (Tmax) of capmatinib

End point description:

Tmax of capmatinib was estimated by non-compartmental analysis. Tmax is the time to reach maximum plasma concentration. Actual recorded sampling times were considered for the calculations. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	55			
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1 (n= 55) Cycle 1 Day 15 (n= 44)	1.87 (0.583 to 4.03) 1.09 (0.5 to 6.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum concentration (Tmax) of CMN288

End point title	Time to reach maximum concentration (Tmax) of CMN288

End point description:

Tmax of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. Tmax is the time to reach maximum plasma concentration. Actual recorded sampling times were considered for the calculations. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from cohorts 1-5, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	51			
Units: hour				
median (full range (min-max))				
Cycle 1 Day 1 (n= 51) Cycle 1 Day 15 (n= 42)	1.93 (0.950 to 4.03) 1.91 (0.883 to 7.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination half-life (T1/2) of capmatinib

End point title	Elimination half-life (T1/2) of capmatinib

End point description:

T1/2 of capmatinib was estimated by non-compartmental analysis. T1/2 is the time it takes for the concentration of capmatinib in the bloodstream to decrease by half. Plasma concentrations of capmatinib were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	47			
Units: hour				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 47) Cycle 1 Day 15 (n= 37)	1.87 (± 0.947) 2.40 (± 0.652)			

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination half-life (T1/2) of CMN288

End point title	Elimination half-life (T1/2) of CMN288

End point description:

T1/2 of CMN288 (metabolite of capmatinib) was estimated by non-compartmental analysis. T1/2 is the time it takes for the concentration of CMN288 in the bloodstream to decrease by half. Plasma concentrations of metabolite CMN288 were measured using validated LCMS/MS methods with a LLOQ of approximately 1.0 ng/mL.
Only a subset of participants from Cohorts 1a, 1b, 2, 3, 4, 5a and 5b, who had an extensive PK collection schedule, were included in this analysis

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Day 15 at pre-dose, 0.5, 1, 2, 4, 6 and 8 hours post-dose. Each Cycle is 21 days

End point values	Cohorts 1-5:Capmatinib administered in fasted state (Full PAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: hour				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 40)	3.14 (± 1.42)			
Cycle 1 Day 15 (n= 34)	3.06 (± 0.949)			

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 start of treatment to 30 days after last dose of treatment. Post-treatment efficacy/survival follow-up deaths were collected from 31 days after last dose of treatment until the end of the study.
All deaths refer to the sum of on-treatment and post-treatment efficacy/survival follow-up deaths.

End point type	Post-hoc

End point timeframe:

On-treatment: Up to approximately 5.5 years. Post-treatment efficacy/survival follow-up: Up to

End point values	Cohort 1a: 2/3L, MET GCN ≥ 10	Cohort 1b: 2/3L, 6 ≤ MET GCN < 10	Cohort 2: 2/3L, 4 ≤ MET GCN < 6	Cohort 3: 2/3L, MET GCN < 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	42	54	30
Units: Participants				
On-treatment	10	7	12	4
Post-treatment efficacy/survival follow-up	44	26	34	22
All deaths	54	33	46	26

End point values	Cohort 4: 2/3L, Mutant	Cohort 5a: 1L, MET GCN ≥10	Cohort 5b: 1L, Mutant	Cohort 6.1 (expansion of Cohort 1a): 2L, MET GCN ≥ 10
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	15	28	3
Units: Participants				
On-treatment	14	0	5	1
Post-treatment efficacy/survival follow-up	44	13	13	2
All deaths	58	13	18	3

End point values	Cohort 6.2 (expansion of Cohort 4): 2L, Mutant	Cohort 7 (expansion of Cohort 5b): 1L, Mutant	Cohort 4 + Cohort 6.2: 2/3L, Mutant	Cohort 5b + Cohort 7: 1L, Mutant
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	32	100	60
Units: Participants				
On-treatment	5	5	19	10
Post-treatment efficacy/survival follow-up	17	16	61	29
All deaths	22	21	80	39

End point values	All participants			
Subject group type	Subject analysis set			
Number of subjects analysed	373			
Units: Participants				
On-treatment	63			
Post-treatment efficacy/survival follow-up	231			

All deaths	294			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from first dose of study treatment to 30 days after last dose of study medication (on-treatment), up to approximately 5.5 years.

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	26.0

Reporting groups

Reporting group title	Cohort 1a: On-treatment

Reporting group description:

AEs collected during the on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 1b: On-treatment

Reporting group description:

AEs collected during the on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 2: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 3: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 5a: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 4: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 5b: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 6.1 (expansion of Cohort 1a): On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 6.2 (expansion of Cohort 4): On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 7 (expansion of Cohort 5b): On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 5b + Cohort 7: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Cohort 4 + Cohort 6.2: On-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	All patients: On-treatment

Reporting group description:

AEs collected during the on-treatment period (up to 30 days post-treatment)

Serious adverse events	Cohort 1a: On-treatment	Cohort 1b: On-treatment	Cohort 2: On-treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 69 (60.87%)	21 / 42 (50.00%)	30 / 54 (55.56%)
number of deaths (all causes)	10	7	12
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Cancer pain			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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
Breast cancer			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 cancer			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Embolism			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Hypertension			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Jugular vein thrombosis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Hypotension			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Thrombosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Superior vena cava syndrome			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Venous thrombosis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Asthenia			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	0 / 54 (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
Drug withdrawal syndrome			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	3 / 69 (4.35%)	3 / 42 (7.14%)	2 / 54 (3.70%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Non-cardiac chest pain			
subjects affected / exposed	2 / 69 (2.90%)	1 / 42 (2.38%)	0 / 54 (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
Pain			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Oedema peripheral			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	0 / 54 (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
Peripheral swelling			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenosis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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
Pyrexia			
subjects affected / exposed	2 / 69 (2.90%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device occlusion			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Genital prolapse			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Scrotal oedema			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Aspiration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Asthma			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 obstructive pulmonary disease			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Dyspnoea			
subjects affected / exposed	6 / 69 (8.70%)	4 / 42 (9.52%)	3 / 54 (5.56%)
occurrences causally related to treatment / all	1 / 6	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			

subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Interstitial lung disease			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Organising pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	6 / 69 (8.70%)	1 / 42 (2.38%)	3 / 54 (5.56%)
occurrences causally related to treatment / all	0 / 7	0 / 1	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Pleuritic pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	0 / 69 (0.00%)	3 / 42 (7.14%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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 haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 venous thrombosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 distress			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 failure			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	0 / 54 (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
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Confusional state			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Anxiety			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Disorientation			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Organic brain syndrome			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Amylase increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 condition abnormal			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Platelet count decreased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
SARS-CoV-2 test positive			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Troponin increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Accidental exposure to product			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Femur fracture			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Lower limb fracture			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Radiation necrosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Toxicity to various agents			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Spinal muscular atrophy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cardiac failure			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Coronary artery disease			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pericardial effusion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Tachycardia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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 ischaemia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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 mass effect			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	1 / 69 (1.45%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Hemiparesis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Neurological symptom			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraplegia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Ear and labyrinth disorders			

Hypoacusis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Vertigo			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
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			
Abdominal pain			
subjects affected / exposed	1 / 69 (1.45%)	2 / 42 (4.76%)	2 / 54 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal prolapse			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Ascites			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Constipation			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Duodenal stenosis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	2 / 69 (2.90%)	0 / 42 (0.00%)	0 / 54 (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
Duodenitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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	1 / 69 (1.45%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	3 / 69 (4.35%)	3 / 42 (7.14%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	2 / 3	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Pancreatitis acute			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Vomiting			

subjects affected / exposed	4 / 69 (5.80%)	2 / 42 (4.76%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	2 / 5	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Hepatitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Urticaria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			

Calculus urinary			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Haematuria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal infarct			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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 retention			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Primary adrenal insufficiency			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
Arthralgia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Back pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Bone pain			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Muscular weakness			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Sacroiliitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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

Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Erysipelas			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Haemophilus infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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
Herpes zoster			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	0 / 69 (0.00%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Lung abscess			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Medical device site infection			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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 infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	7 / 69 (10.14%)	4 / 42 (9.52%)	3 / 54 (5.56%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 bacterial			

subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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 tract infection			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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
Septic shock			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Urosepsis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (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
Hypokalaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (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	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (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	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 3: On-treatment	Cohort 5a: On-treatment	Cohort 4: On-treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 30 (50.00%)	9 / 15 (60.00%)	38 / 69 (55.07%)
number of deaths (all causes)	4	0	14
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Cancer pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Breast cancer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 cancer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Tumour pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Tumour haemorrhage			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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			
Embolism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Hypertension			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Jugular vein thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Hypotension			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Drug withdrawal syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Fatigue			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	1 / 30 (3.33%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Generalised oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Oedema peripheral			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Peripheral swelling			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device occlusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Genital prolapse			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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

Asthma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Haemoptysis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	2 / 30 (6.67%)	1 / 15 (6.67%)	6 / 69 (8.70%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Interstitial lung disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Pleuritic pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
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 embolism			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	0 / 69 (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
Pneumothorax			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Pneumonitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pulmonary haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 venous thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 failure			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Anxiety			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Disorientation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Mental status changes			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Organic brain syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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			
Amylase increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Eastern Cooperative Oncology Group			

performance status worsened			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Liver function test abnormal			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Platelet count decreased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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			
Accidental exposure to product			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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

Fracture displacement			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Lower limb fracture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Thoracic vertebral fracture			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Toxicity to various agents			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Congenital, familial and genetic disorders			
Spinal muscular atrophy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 arrest			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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

Cardiac failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Coronary artery disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 infarction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Pericardial effusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 ischaemia			

subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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 mass effect			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Neurological symptom			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Seizure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Paraplegia			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Thrombocytopenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Anal prolapse			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 upper			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Ascites			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Constipation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal stenosis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Dysphagia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 polyp			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Pancreatitis acute			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Stomatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Hepatitis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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			
Urticaria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 infarct			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 retention			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Primary adrenal insufficiency			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Bone pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
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	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
Osteolysis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sacroiliitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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
COVID-19			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Haemophilus infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Herpes zoster			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Lung abscess			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Medical device site infection			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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	1 / 30 (3.33%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	0 / 69 (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
Sepsis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Septic shock			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	0 / 69 (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
Urosepsis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (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			
Decreased appetite			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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
Hyperkalaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (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 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (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

Serious adverse events	Cohort 5b: On-treatment	Cohort 6.1 (expansion of Cohort 1a): On-treatment	Cohort 6.2 (expansion of Cohort 4): On-treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 28 (50.00%)	2 / 3 (66.67%)	14 / 31 (45.16%)
number of deaths (all causes)	5	1	5
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Cancer pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Breast cancer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Tumour pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Tumour haemorrhage			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Jugular vein thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Hypotension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Superior vena cava syndrome			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Venous thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Asthenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Drug withdrawal syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Fatigue			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Malaise			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Generalised oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Non-cardiac chest pain			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Peripheral swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Stenosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device occlusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Genital prolapse			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Scrotal oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Aspiration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Asthma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 obstructive pulmonary disease			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Haemoptysis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Interstitial lung disease			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Organising pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pleural effusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Pleuritic pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Pneumothorax			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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 haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
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 venous thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 distress			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Respiratory failure			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Confusional state			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Anxiety			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Disorientation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Mental status changes			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Organic brain syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Amylase increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 condition abnormal			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 31 (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
Liver function test abnormal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Platelet count decreased			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Troponin increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Accidental exposure to product			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Femur fracture			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Fracture displacement			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Radiation necrosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Thoracic vertebral fracture			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Toxicity to various agents			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Congenital, familial and genetic disorders			
Spinal muscular atrophy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 failure			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Coronary artery disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 infarction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 ischaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 mass effect			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Hemiparesis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Neurological symptom			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Paraplegia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Thrombocytopenia			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Vertigo			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Abdominal pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal prolapse			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 upper			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Ascites			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Duodenal stenosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Duodenitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Pancreatitis acute			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Drug-induced liver injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Calculus urinary			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 infarct			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 retention			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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

Primary adrenal insufficiency			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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			
Arthralgia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Back pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Bone pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Osteolysis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Sacroiliitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
COVID-19			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Erysipelas			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Haemophilus infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Herpes zoster			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
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 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Lung abscess			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Medical device site infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	1 / 3 (33.33%)	2 / 31 (6.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia influenzal			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 bacterial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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
Pyelonephritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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 tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Septic shock			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Urosepsis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Hypokalaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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
Hyperkalaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (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	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (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

Serious adverse events	Cohort 7 (expansion of Cohort 5b): On-treatment	Cohort 5b + Cohort 7: On-treatment	Cohort 4 + Cohort 6.2: On-treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 32 (53.13%)	31 / 60 (51.67%)	52 / 100 (52.00%)
number of deaths (all causes)	5	10	19
number of deaths resulting from adverse events	0	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			

subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Tumour pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Hypertension			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Jugular vein thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Hypotension			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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			
Asthenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Drug withdrawal syndrome			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Fatigue			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
General physical health deterioration			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Generalised oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device occlusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Genital prolapse			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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			

Acute respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Asthma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Haemoptysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 32 (3.13%)	3 / 60 (5.00%)	7 / 100 (7.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Interstitial lung disease			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pleural effusion			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	3 / 100 (3.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Pleuritic pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Pneumothorax			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	3 / 100 (3.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pulmonary haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary venous thrombosis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Anxiety			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Disorientation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Mental status changes			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Organic brain syndrome			

subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Investigations			
Amylase increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Liver function test abnormal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Platelet count decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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			

Accidental exposure to product			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Fracture displacement			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Toxicity to various agents			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Congenital, familial and genetic disorders			
Spinal muscular atrophy			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 failure			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Cardiopulmonary failure			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 infarction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 ischaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 mass effect			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Neurological symptom			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Paraplegia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Thrombocytopenia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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			

Abdominal pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal prolapse			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 upper			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Ascites			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Diarrhoea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal stenosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Pancreatitis acute			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	1 / 32 (3.13%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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 function abnormal			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 infarct			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 retention			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Primary adrenal insufficiency			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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			
Arthralgia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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

Bone pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Muscular weakness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Osteolysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sacroiliitis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (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
Pain in extremity			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
COVID-19			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	1 / 60 (1.67%)	4 / 100 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophilus infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Herpes zoster			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Lung abscess			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Medical device site infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	1 / 32 (3.13%)	1 / 60 (1.67%)	6 / 100 (6.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (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			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Septic shock			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Urosepsis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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
Hyperkalaemia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (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 / 32 (3.13%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All patients: On-treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	202 / 373 (54.16%)		
number of deaths (all causes)	63		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal cancer			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Tumour pain				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Embolism				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jugular vein thrombosis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombosis				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Superior vena cava syndrome				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Drug withdrawal syndrome				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	11 / 373 (2.95%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	4 / 373 (1.07%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	6 / 373 (1.61%)			
occurrences causally related to treatment / all	4 / 8			
deaths causally related to treatment / all	0 / 0			
Peripheral swelling				
subjects affected / exposed	4 / 373 (1.07%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Stenosis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	5 / 373 (1.34%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Vascular device occlusion				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Breast pain				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Genital prolapse				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scrotal oedema				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic pain				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspiration				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Asthma				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				

subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	26 / 373 (6.97%)			
occurrences causally related to treatment / all	1 / 31			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Pleural effusion				
subjects affected / exposed	16 / 373 (4.29%)			
occurrences causally related to treatment / all	4 / 19			
deaths causally related to treatment / all	0 / 0			
Pleurisy				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	7 / 373 (1.88%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	4 / 373 (1.07%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	6 / 373 (1.61%)			
occurrences causally related to treatment / all	3 / 6			
deaths causally related to treatment / all	1 / 1			
Pulmonary haemorrhage				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary venous thrombosis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	5 / 373 (1.34%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Agitation				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				

subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Organic brain syndrome				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Amylase increased				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eastern Cooperative Oncology Group performance status worsened				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical condition abnormal				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
SARS-CoV-2 test positive				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Troponin increased				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Accidental exposure to product				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Fracture displacement				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radiation necrosis				

subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thoracic vertebral fracture			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxicity to various agents			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Spinal muscular atrophy			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Cardiac arrest			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Cardiac failure			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Cardiopulmonary failure			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Coronary artery disease				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Aphasia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cerebral mass effect				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological symptom				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Paraplegia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Hypoacusis				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Vertigo				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	6 / 373 (1.61%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Anal prolapse				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenal stenosis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	7 / 373 (1.88%)			
occurrences causally related to treatment / all	5 / 7			
deaths causally related to treatment / all	0 / 0			
Intestinal polyp				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal stenosis				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	9 / 373 (2.41%)			
occurrences causally related to treatment / all	6 / 10			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic function abnormal				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Hepatotoxicity				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				

subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Renal infarct			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			

Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Primary adrenal insufficiency				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	4 / 373 (1.07%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Osteolysis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Sacroiliitis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bronchitis				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	6 / 373 (1.61%)			
occurrences causally related to treatment / all	2 / 6			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemophilus infection				

subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Infectious pleural effusion				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Medical device site infection				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural infection				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	23 / 373 (6.17%)		
occurrences causally related to treatment / all	1 / 25		
deaths causally related to treatment / all	0 / 1		
Pneumonia influenzal			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia aspiration			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Septic shock			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			

subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	2 / 373 (0.54%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	6 / 373 (1.61%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Cohort 1a: On-treatment	Cohort 1b: On-treatment	Cohort 2: On-treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 69 (95.65%)	41 / 42 (97.62%)	53 / 54 (98.15%)
Vascular disorders			
Hypotension			
subjects affected / exposed	4 / 69 (5.80%)	1 / 42 (2.38%)	2 / 54 (3.70%)
occurrences (all)	4	1	2
Embolism			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	4 / 69 (5.80%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	4	0	1
Deep vein thrombosis			
subjects affected / exposed	0 / 69 (0.00%)	2 / 42 (4.76%)	2 / 54 (3.70%)
occurrences (all)	0	2	2
Superficial vein thrombosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	11 / 69 (15.94%)	10 / 42 (23.81%)	16 / 54 (29.63%)
occurrences (all)	11	10	18
Face oedema			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1
Chest discomfort			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	1	1	1
Asthenia			
subjects affected / exposed	6 / 69 (8.70%)	8 / 42 (19.05%)	11 / 54 (20.37%)
occurrences (all)	7	9	11
Malaise			

subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1
Pyrexia			
subjects affected / exposed	8 / 69 (11.59%)	7 / 42 (16.67%)	8 / 54 (14.81%)
occurrences (all)	11	9	9
Peripheral swelling			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	2	3	2
Non-cardiac chest pain			
subjects affected / exposed	8 / 69 (11.59%)	5 / 42 (11.90%)	7 / 54 (12.96%)
occurrences (all)	10	6	8
Oedema			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	34 / 69 (49.28%)	18 / 42 (42.86%)	24 / 54 (44.44%)
occurrences (all)	53	28	37
Pain			
subjects affected / exposed	4 / 69 (5.80%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	4	0	1
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Breast swelling			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	9 / 69 (13.04%)	9 / 42 (21.43%)	9 / 54 (16.67%)
occurrences (all)	14	10	9
Dysphonia			
subjects affected / exposed	4 / 69 (5.80%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	4	1	0
Interstitial lung disease			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	3 / 69 (4.35%)	3 / 42 (7.14%)	3 / 54 (5.56%)
occurrences (all)	3	3	3
Epistaxis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Emphysema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	11 / 69 (15.94%)	15 / 42 (35.71%)	11 / 54 (20.37%)
occurrences (all)	12	17	15
Rhinitis allergic			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	1 / 69 (1.45%)	4 / 42 (9.52%)	2 / 54 (3.70%)
occurrences (all)	2	4	2
Productive cough			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences (all)	3	0	2

Pneumonitis			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	4	0	0
Pleurisy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	3 / 69 (4.35%)	4 / 42 (9.52%)	3 / 54 (5.56%)
occurrences (all)	3	9	4
Oropharyngeal pain			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	1	1	1
Rhinorrhoea			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 69 (10.14%)	3 / 42 (7.14%)	3 / 54 (5.56%)
occurrences (all)	7	3	3
Dysphoria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	2 / 54 (3.70%)
occurrences (all)	1	1	2
Confusional state			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	0 / 69 (0.00%)	3 / 42 (7.14%)	4 / 54 (7.41%)
occurrences (all)	0	3	4
Sleep disorder			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	1	1	1
Investigations			

Amylase increased			
subjects affected / exposed	9 / 69 (13.04%)	3 / 42 (7.14%)	2 / 54 (3.70%)
occurrences (all)	15	4	2
Alanine aminotransferase increased			
subjects affected / exposed	13 / 69 (18.84%)	4 / 42 (9.52%)	5 / 54 (9.26%)
occurrences (all)	17	4	5
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 69 (15.94%)	2 / 42 (4.76%)	4 / 54 (7.41%)
occurrences (all)	14	3	5
Blood urine present			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	16 / 69 (23.19%)	8 / 42 (19.05%)	14 / 54 (25.93%)
occurrences (all)	55	11	26
Blood bilirubin increased			
subjects affected / exposed	3 / 69 (4.35%)	2 / 42 (4.76%)	1 / 54 (1.85%)
occurrences (all)	11	2	2
Blood alkaline phosphatase increased			
subjects affected / exposed	8 / 69 (11.59%)	1 / 42 (2.38%)	3 / 54 (5.56%)
occurrences (all)	9	1	3
Blood albumin decreased			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	3	0	2
Liver function test abnormal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	5 / 69 (7.25%)	4 / 42 (9.52%)	1 / 54 (1.85%)
occurrences (all)	8	5	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	9 / 69 (13.04%)	2 / 42 (4.76%)	5 / 54 (9.26%)
occurrences (all)	13	2	6
Eastern Cooperative Oncology Group performance status worsened			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	3 / 69 (4.35%)	2 / 42 (4.76%)	0 / 54 (0.00%)
occurrences (all)	3	2	0
Liver function test increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences (all)	3	0	2
Platelet count decreased			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	3 / 54 (5.56%)
occurrences (all)	8	0	3
Procalcitonin increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	7 / 69 (10.14%)	4 / 42 (9.52%)	2 / 54 (3.70%)
occurrences (all)	7	4	2
Weight increased			
subjects affected / exposed	7 / 69 (10.14%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences (all)	7	0	2
White blood cell count decreased			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
Anastomotic ulcer			

subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Face injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	1	0	3
Head injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Pelvic fracture			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Spinal compression fracture			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 69 (0.00%)	3 / 42 (7.14%)	0 / 54 (0.00%)
occurrences (all)	0	4	0
Sinus bradycardia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	1	1	1
Cardiac failure			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences (all)	2	0	3

Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	4 / 69 (5.80%)	5 / 42 (11.90%)	1 / 54 (1.85%)
occurrences (all)	4	5	1
Paraesthesia			
subjects affected / exposed	1 / 69 (1.45%)	3 / 42 (7.14%)	2 / 54 (3.70%)
occurrences (all)	2	3	2
Neuropathy peripheral			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	4	1	0
Headache			
subjects affected / exposed	6 / 69 (8.70%)	4 / 42 (9.52%)	3 / 54 (5.56%)
occurrences (all)	7	6	3
Dysgeusia			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	3	0	0
Dysarthria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1
Syncope			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	0	1	1
Taste disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Tremor			

subjects affected / exposed	0 / 69 (0.00%)	2 / 42 (4.76%)	2 / 54 (3.70%)
occurrences (all)	0	3	2
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	4	0	1
Thrombocytopenia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	5 / 69 (7.25%)	2 / 42 (4.76%)	5 / 54 (9.26%)
occurrences (all)	5	2	8
Leukopenia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences (all)	2	0	2
Lymphopenia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	2 / 69 (2.90%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	2	1	1
Tinnitus			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	2 / 69 (2.90%)	2 / 42 (4.76%)	2 / 54 (3.70%)
occurrences (all)	2	2	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 69 (2.90%)	3 / 42 (7.14%)	7 / 54 (12.96%)
occurrences (all)	2	4	8
Abdominal discomfort			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			

subjects affected / exposed	4 / 69 (5.80%)	4 / 42 (9.52%)	2 / 54 (3.70%)
occurrences (all)	4	6	2
Abnormal faeces			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	32 / 69 (46.38%)	16 / 42 (38.10%)	24 / 54 (44.44%)
occurrences (all)	42	21	26
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 69 (4.35%)	1 / 42 (2.38%)	3 / 54 (5.56%)
occurrences (all)	3	1	3
Dysphagia			
subjects affected / exposed	2 / 69 (2.90%)	4 / 42 (9.52%)	6 / 54 (11.11%)
occurrences (all)	2	4	7
Dyspepsia			
subjects affected / exposed	4 / 69 (5.80%)	3 / 42 (7.14%)	4 / 54 (7.41%)
occurrences (all)	4	3	4
Dry mouth			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	18 / 69 (26.09%)	6 / 42 (14.29%)	7 / 54 (12.96%)
occurrences (all)	24	8	12
Constipation			
subjects affected / exposed	16 / 69 (23.19%)	9 / 42 (21.43%)	10 / 54 (18.52%)
occurrences (all)	16	10	10
Vomiting			
subjects affected / exposed	22 / 69 (31.88%)	14 / 42 (33.33%)	12 / 54 (22.22%)
occurrences (all)	34	16	17
Stomatitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	3 / 54 (5.56%)
occurrences (all)	1	0	3
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	9 / 69 (13.04%)	1 / 42 (2.38%)	2 / 54 (3.70%)
occurrences (all)	9	2	2
Eczema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	7 / 69 (10.14%)	6 / 42 (14.29%)	3 / 54 (5.56%)
occurrences (all)	7	6	4
Pruritus allergic			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	3 / 69 (4.35%)	1 / 42 (2.38%)	4 / 54 (7.41%)
occurrences (all)	3	2	4
Rash maculo-papular			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	2 / 54 (3.70%)
occurrences (all)	2	0	2
Alopecia			
subjects affected / exposed	0 / 69 (0.00%)	3 / 42 (7.14%)	0 / 54 (0.00%)
occurrences (all)	0	3	0
Dermatitis acneiform			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	1	0	1
Skin induration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Stasis dermatitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	1	1	0
Dysuria			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	1	0	2
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 69 (1.45%)	3 / 42 (7.14%)	0 / 54 (0.00%)
occurrences (all)	1	4	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 69 (8.70%)	3 / 42 (7.14%)	7 / 54 (12.96%)
occurrences (all)	7	3	12
Muscle spasms			
subjects affected / exposed	4 / 69 (5.80%)	6 / 42 (14.29%)	3 / 54 (5.56%)
occurrences (all)	4	7	3
Joint swelling			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	8 / 69 (11.59%)	7 / 42 (16.67%)	10 / 54 (18.52%)
occurrences (all)	8	7	10
Muscular weakness			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	1	1	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 69 (2.90%)	1 / 42 (2.38%)	3 / 54 (5.56%)
occurrences (all)	2	1	3
Musculoskeletal pain			
subjects affected / exposed	3 / 69 (4.35%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	4	1	1
Pain in extremity			

subjects affected / exposed	6 / 69 (8.70%)	2 / 42 (4.76%)	3 / 54 (5.56%)
occurrences (all)	7	3	3
Neck pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	4 / 69 (5.80%)	3 / 42 (7.14%)	1 / 54 (1.85%)
occurrences (all)	4	3	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	3 / 54 (5.56%)
occurrences (all)	1	1	4
Influenza			
subjects affected / exposed	0 / 69 (0.00%)	3 / 42 (7.14%)	1 / 54 (1.85%)
occurrences (all)	0	3	1
Herpes zoster			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Erysipelas			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Epididymitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	3 / 69 (4.35%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	3	0	1
COVID-19			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 69 (10.14%)	4 / 42 (9.52%)	1 / 54 (1.85%)
occurrences (all)	7	6	2
Staphylococcal infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0

Sepsis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	0	1	0
Pyuria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	6 / 69 (8.70%)	5 / 42 (11.90%)	1 / 54 (1.85%)
occurrences (all)	8	5	1
Oral candidiasis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	3 / 54 (5.56%)
occurrences (all)	0	0	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 42 (2.38%)	1 / 54 (1.85%)
occurrences (all)	0	1	2
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	4 / 54 (7.41%)
occurrences (all)	2	1	4
Hypoalbuminaemia			
subjects affected / exposed	9 / 69 (13.04%)	4 / 42 (9.52%)	5 / 54 (9.26%)
occurrences (all)	12	6	7
Hypocalcaemia			
subjects affected / exposed	1 / 69 (1.45%)	1 / 42 (2.38%)	0 / 54 (0.00%)
occurrences (all)	1	2	0
Hypercalcaemia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 42 (0.00%)	3 / 54 (5.56%)
occurrences (all)	1	0	3
Decreased appetite			

subjects affected / exposed	15 / 69 (21.74%)	6 / 42 (14.29%)	12 / 54 (22.22%)
occurrences (all)	16	6	12
Hypokalaemia			
subjects affected / exposed	5 / 69 (7.25%)	2 / 42 (4.76%)	2 / 54 (3.70%)
occurrences (all)	6	5	2
Hypomagnesaemia			
subjects affected / exposed	2 / 69 (2.90%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1
Hypophosphataemia			
subjects affected / exposed	9 / 69 (13.04%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	12	0	1
Hypophagia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 42 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	1 / 69 (1.45%)	2 / 42 (4.76%)	3 / 54 (5.56%)
occurrences (all)	1	2	3

Non-serious adverse events	Cohort 3: On-treatment	Cohort 5a: On-treatment	Cohort 4: On-treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 30 (93.33%)	15 / 15 (100.00%)	66 / 69 (95.65%)
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	5 / 69 (7.25%)
occurrences (all)	1	0	7
Embolism			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences (all)	1	1	2
Deep vein thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Superficial vein thrombosis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	6 / 30 (20.00%)	2 / 15 (13.33%)	19 / 69 (27.54%)
occurrences (all)	6	5	22
Face oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	0	0	4
Chest discomfort			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	3 / 30 (10.00%)	2 / 15 (13.33%)	6 / 69 (8.70%)
occurrences (all)	3	3	11
Malaise			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	4
Pyrexia			
subjects affected / exposed	5 / 30 (16.67%)	3 / 15 (20.00%)	9 / 69 (13.04%)
occurrences (all)	9	4	11
Peripheral swelling			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	1	1	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 30 (3.33%)	3 / 15 (20.00%)	4 / 69 (5.80%)
occurrences (all)	1	3	6
Oedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	11 / 30 (36.67%)	10 / 15 (66.67%)	38 / 69 (55.07%)
occurrences (all)	12	15	71
Pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	1	0	2
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Breast swelling			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Breast pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 30 (13.33%)	2 / 15 (13.33%)	11 / 69 (15.94%)
occurrences (all)	4	2	13
Dysphonia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	1	0	3
Interstitial lung disease			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Hypoxia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Haemoptysis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Epistaxis			

subjects affected / exposed	1 / 30 (3.33%)	2 / 15 (13.33%)	3 / 69 (4.35%)
occurrences (all)	1	2	3
Emphysema			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	3 / 69 (4.35%)
occurrences (all)	1	1	4
Dyspnoea			
subjects affected / exposed	5 / 30 (16.67%)	5 / 15 (33.33%)	16 / 69 (23.19%)
occurrences (all)	8	5	17
Rhinitis allergic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 30 (0.00%)	2 / 15 (13.33%)	2 / 69 (2.90%)
occurrences (all)	0	2	2
Productive cough			
subjects affected / exposed	4 / 30 (13.33%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	4	0	4
Pneumonitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	1	0	6
Pleurisy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	4
Oropharyngeal pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	1	0	2
Psychiatric disorders			

Insomnia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	6 / 69 (8.70%)
occurrences (all)	1	0	7
Dysphoria			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	3
Confusional state			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	1	1	0
Anxiety			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	3 / 69 (4.35%)
occurrences (all)	0	1	3
Sleep disorder			
subjects affected / exposed	0 / 30 (0.00%)	2 / 15 (13.33%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Investigations			
Amylase increased			
subjects affected / exposed	1 / 30 (3.33%)	3 / 15 (20.00%)	7 / 69 (10.14%)
occurrences (all)	1	3	10
Alanine aminotransferase increased			
subjects affected / exposed	3 / 30 (10.00%)	5 / 15 (33.33%)	9 / 69 (13.04%)
occurrences (all)	3	7	9
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 30 (10.00%)	5 / 15 (33.33%)	6 / 69 (8.70%)
occurrences (all)	3	6	8
Blood urine present			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	5 / 30 (16.67%)	3 / 15 (20.00%)	24 / 69 (34.78%)
occurrences (all)	9	7	55
Blood bilirubin increased			

subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	5 / 69 (7.25%)
occurrences (all)	0	1	6
Blood albumin decreased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	5 / 69 (7.25%)
occurrences (all)	1	1	8
Liver function test abnormal			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	1	1	0
Lipase increased			
subjects affected / exposed	4 / 30 (13.33%)	1 / 15 (6.67%)	7 / 69 (10.14%)
occurrences (all)	6	1	17
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	4
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	2	0	0
Liver function test increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences (all)	2	1	7
Platelet count decreased			

subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	5 / 69 (7.25%)
occurrences (all)	1	1	14
Procalcitonin increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	4 / 30 (13.33%)	3 / 15 (20.00%)	9 / 69 (13.04%)
occurrences (all)	4	3	11
Weight increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	4 / 69 (5.80%)
occurrences (all)	0	2	4
White blood cell count decreased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	4	1	1
Injury, poisoning and procedural complications			
Anastomotic ulcer			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Face injury			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences (all)	0	1	2
Head injury			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Pelvic fracture			

subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Spinal compression fracture			
subjects affected / exposed	0 / 30 (0.00%)	2 / 15 (13.33%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Sinus bradycardia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	0	0	4
Palpitations			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences (all)	0	2	2
Cardiac failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences (all)	0	1	2
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)	2 / 15 (13.33%)	9 / 69 (13.04%)
occurrences (all)	2	2	9
Paraesthesia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	3
Neuropathy peripheral			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Hypoaesthesia			

subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	2 / 69 (2.90%)
occurrences (all)	1	1	2
Headache			
subjects affected / exposed	2 / 30 (6.67%)	1 / 15 (6.67%)	9 / 69 (13.04%)
occurrences (all)	2	1	9
Dysgeusia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Syncope			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	1	1	3
Thrombocytopenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	4
Anaemia			
subjects affected / exposed	6 / 30 (20.00%)	1 / 15 (6.67%)	8 / 69 (11.59%)
occurrences (all)	10	1	8
Leukopenia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	1	1	0

Lymphopenia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	2	0	1
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	3
Tinnitus			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	5 / 69 (7.25%)
occurrences (all)	2	0	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	1	0	7
Abdominal discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	5 / 69 (7.25%)
occurrences (all)	2	0	6
Abnormal faeces			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	15 / 30 (50.00%)	9 / 15 (60.00%)	32 / 69 (46.38%)
occurrences (all)	18	12	48
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 30 (3.33%)	2 / 15 (13.33%)	1 / 69 (1.45%)
occurrences (all)	1	2	1
Dyspepsia			

subjects affected / exposed	3 / 30 (10.00%)	0 / 15 (0.00%)	6 / 69 (8.70%)
occurrences (all)	4	0	6
Dry mouth			
subjects affected / exposed	2 / 30 (6.67%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	8 / 30 (26.67%)	4 / 15 (26.67%)	13 / 69 (18.84%)
occurrences (all)	8	4	16
Constipation			
subjects affected / exposed	7 / 30 (23.33%)	6 / 15 (40.00%)	9 / 69 (13.04%)
occurrences (all)	8	6	11
Vomiting			
subjects affected / exposed	9 / 30 (30.00%)	4 / 15 (26.67%)	19 / 69 (27.54%)
occurrences (all)	13	5	38
Stomatitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	3 / 69 (4.35%)
occurrences (all)	0	1	3
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 30 (3.33%)	2 / 15 (13.33%)	2 / 69 (2.90%)
occurrences (all)	1	3	2
Eczema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 30 (0.00%)	2 / 15 (13.33%)	10 / 69 (14.49%)
occurrences (all)	0	2	12
Pruritus allergic			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Rash			

subjects affected / exposed	1 / 30 (3.33%)	2 / 15 (13.33%)	6 / 69 (8.70%)
occurrences (all)	1	2	6
Rash maculo-papular			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	3
Skin induration			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Stasis dermatitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 30 (0.00%)	3 / 15 (20.00%)	8 / 69 (11.59%)
occurrences (all)	0	3	11
Muscle spasms			

subjects affected / exposed	1 / 30 (3.33%)	3 / 15 (20.00%)	1 / 69 (1.45%)
occurrences (all)	1	3	1
Joint swelling			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	2 / 30 (6.67%)	2 / 15 (13.33%)	11 / 69 (15.94%)
occurrences (all)	2	2	13
Muscular weakness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 30 (6.67%)	1 / 15 (6.67%)	6 / 69 (8.70%)
occurrences (all)	2	1	7
Musculoskeletal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	7 / 69 (10.14%)
occurrences (all)	1	1	9
Neck pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	0	0	4
Myalgia			
subjects affected / exposed	1 / 30 (3.33%)	2 / 15 (13.33%)	5 / 69 (7.25%)
occurrences (all)	1	2	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	0	0	4
Influenza			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0

Herpes zoster			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Epididymitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	4 / 69 (5.80%)
occurrences (all)	0	0	7
COVID-19			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 15 (6.67%)	3 / 69 (4.35%)
occurrences (all)	1	1	4
Staphylococcal infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Sepsis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Pyuria			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	3 / 30 (10.00%)	1 / 15 (6.67%)	5 / 69 (7.25%)
occurrences (all)	3	2	6
Oral candidiasis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	7 / 69 (10.14%)
occurrences (all)	0	0	9
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	5 / 69 (7.25%)
occurrences (all)	0	1	11
Hypocalcaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	5 / 69 (7.25%)
occurrences (all)	0	1	5
Hypercalcaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Decreased appetite			
subjects affected / exposed	8 / 30 (26.67%)	4 / 15 (26.67%)	15 / 69 (21.74%)
occurrences (all)	9	4	20
Hypokalaemia			
subjects affected / exposed	3 / 30 (10.00%)	1 / 15 (6.67%)	3 / 69 (4.35%)
occurrences (all)	3	1	3
Hypomagnesaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 15 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	3
Hypophagia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 15 (6.67%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			

subjects affected / exposed	0 / 30 (0.00%)	2 / 15 (13.33%)	3 / 69 (4.35%)
occurrences (all)	0	2	4

Non-serious adverse events	Cohort 5b: On-treatment	Cohort 6.1 (expansion of Cohort 1a): On-treatment	Cohort 6.2 (expansion of Cohort 4): On-treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)	3 / 3 (100.00%)	29 / 31 (93.55%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Embolism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2
Deep vein thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Superficial vein thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	4 / 28 (14.29%)	1 / 3 (33.33%)	11 / 31 (35.48%)
occurrences (all)	5	1	12
Face oedema			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Chest discomfort			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0

Asthenia			
subjects affected / exposed	4 / 28 (14.29%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	4	0	4
Malaise			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	2 / 31 (6.45%)
occurrences (all)	2	1	2
Peripheral swelling			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Oedema			
subjects affected / exposed	4 / 28 (14.29%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	5	0	0
Oedema peripheral			
subjects affected / exposed	21 / 28 (75.00%)	1 / 3 (33.33%)	23 / 31 (74.19%)
occurrences (all)	45	1	46
Pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Breast swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Breast pain			

subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 28 (25.00%)	0 / 3 (0.00%)	7 / 31 (22.58%)
occurrences (all)	9	0	8
Dysphonia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Interstitial lung disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2
Haemoptysis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	3 / 31 (9.68%)
occurrences (all)	1	1	5
Epistaxis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Emphysema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	6 / 28 (21.43%)	2 / 3 (66.67%)	6 / 31 (19.35%)
occurrences (all)	8	2	6
Rhinitis allergic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	4
Pulmonary embolism			

subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Productive cough			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	5	0	1
Pneumonitis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Pleurisy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	2
Pleural effusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	3 / 31 (9.68%)
occurrences (all)	0	1	3
Rhinorrhoea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	4
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 28 (17.86%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	5	0	3
Dysphoria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Confusional state			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1

Sleep disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	4 / 31 (12.90%)
occurrences (all)	2	0	7
Alanine aminotransferase increased			
subjects affected / exposed	4 / 28 (14.29%)	0 / 3 (0.00%)	7 / 31 (22.58%)
occurrences (all)	5	0	9
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	4 / 31 (12.90%)
occurrences (all)	2	0	5
Blood urine present			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	10 / 28 (35.71%)	1 / 3 (33.33%)	10 / 31 (32.26%)
occurrences (all)	13	3	15
Blood bilirubin increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	4	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	4
Blood albumin decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	5 / 28 (17.86%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	5	0	15
Gamma-glutamyltransferase increased			

subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	2	0	3
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Liver function test increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Platelet count decreased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	1 / 31 (3.23%)
occurrences (all)	2	2	2
Procalcitonin increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	3
Weight decreased			
subjects affected / exposed	4 / 28 (14.29%)	1 / 3 (33.33%)	1 / 31 (3.23%)
occurrences (all)	4	2	1
Weight increased			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	3	0	2
White blood cell count decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0

Injury, poisoning and procedural complications			
Anastomotic ulcer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Face injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2
Head injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Pelvic fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Cardiac failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	3 / 31 (9.68%)
occurrences (all)	4	2	7
Paraesthesia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Neuropathy peripheral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	3
Dysgeusia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Taste disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1

Tremor			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	8
Anaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	4 / 31 (12.90%)
occurrences (all)	2	0	5
Leukopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Tinnitus			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	3	0	3
Vertigo			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	4	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			

subjects affected / exposed	5 / 28 (17.86%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	5	0	2
Abnormal faeces			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	13 / 28 (46.43%)	2 / 3 (66.67%)	12 / 31 (38.71%)
occurrences (all)	19	2	16
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	2
Dysphagia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	1 / 31 (3.23%)
occurrences (all)	2	1	1
Dry mouth			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	5 / 28 (17.86%)	0 / 3 (0.00%)	5 / 31 (16.13%)
occurrences (all)	7	0	6
Constipation			
subjects affected / exposed	5 / 28 (17.86%)	1 / 3 (33.33%)	3 / 31 (9.68%)
occurrences (all)	5	2	3
Vomiting			
subjects affected / exposed	7 / 28 (25.00%)	1 / 3 (33.33%)	8 / 31 (25.81%)
occurrences (all)	9	1	8
Stomatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1

Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Pruritus			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	2	0	5
Pruritus allergic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
Rash maculo-papular			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Alopecia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Dermatitis acneiform			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	2
Skin induration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Stasis dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 28 (25.00%)	1 / 3 (33.33%)	2 / 31 (6.45%)
occurrences (all)	7	1	3
Muscle spasms			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	4	0	3
Joint swelling			
subjects affected / exposed	2 / 28 (7.14%)	1 / 3 (33.33%)	1 / 31 (3.23%)
occurrences (all)	2	1	1
Flank pain			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	1 / 31 (3.23%)
occurrences (all)	1	1	1
Back pain			
subjects affected / exposed	4 / 28 (14.29%)	1 / 3 (33.33%)	11 / 31 (35.48%)
occurrences (all)	5	1	13
Muscular weakness			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Musculoskeletal chest pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			

subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	5 / 31 (16.13%)
occurrences (all)	3	0	7
Neck pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Erysipelas			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Epididymitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	3	0	3
COVID-19			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Nasopharyngitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	3 / 31 (9.68%)
occurrences (all)	3	0	4
Staphylococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Sepsis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Pyuria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	6
Oral candidiasis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	6 / 31 (19.35%)
occurrences (all)	3	0	7
Hypocalcaemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	4 / 31 (12.90%)
occurrences (all)	5	0	5
Hypercalcaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			

subjects affected / exposed	8 / 28 (28.57%)	0 / 3 (0.00%)	6 / 31 (19.35%)
occurrences (all)	9	0	6
Hypokalaemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	3
Hypomagnesaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	4 / 31 (12.90%)
occurrences (all)	4	0	10
Hypophagia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 3 (33.33%)	0 / 31 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	Cohort 7 (expansion of Cohort 5b): On-treatment	Cohort 5b + Cohort 7: On-treatment	Cohort 4 + Cohort 6.2: On-treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 32 (96.88%)	59 / 60 (98.33%)	95 / 100 (95.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 32 (15.63%)	5 / 60 (8.33%)	6 / 100 (6.00%)
occurrences (all)	7	7	8
Embolism			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	1	1	2
Hypertension			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	4 / 100 (4.00%)
occurrences (all)	1	3	4
Deep vein thrombosis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	2 / 100 (2.00%)
occurrences (all)	2	2	2
Superficial vein thrombosis			

subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences (all)	2	2	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	2 / 100 (2.00%)
occurrences (all)	4	5	2
Fatigue			
subjects affected / exposed	6 / 32 (18.75%)	10 / 60 (16.67%)	30 / 100 (30.00%)
occurrences (all)	6	11	34
Face oedema			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	5 / 100 (5.00%)
occurrences (all)	0	2	5
Chest discomfort			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	6 / 32 (18.75%)	10 / 60 (16.67%)	9 / 100 (9.00%)
occurrences (all)	6	10	15
Malaise			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	4 / 100 (4.00%)
occurrences (all)	0	2	5
Pyrexia			
subjects affected / exposed	4 / 32 (12.50%)	6 / 60 (10.00%)	11 / 100 (11.00%)
occurrences (all)	8	10	13
Peripheral swelling			
subjects affected / exposed	3 / 32 (9.38%)	4 / 60 (6.67%)	1 / 100 (1.00%)
occurrences (all)	5	6	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	7 / 100 (7.00%)
occurrences (all)	0	1	9
Oedema			
subjects affected / exposed	3 / 32 (9.38%)	7 / 60 (11.67%)	0 / 100 (0.00%)
occurrences (all)	3	8	0
Oedema peripheral			

subjects affected / exposed	23 / 32 (71.88%)	44 / 60 (73.33%)	61 / 100 (61.00%)
occurrences (all)	35	80	117
Pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	1	1	2
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	1 / 32 (3.13%)	3 / 60 (5.00%)	0 / 100 (0.00%)
occurrences (all)	2	4	0
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	1 / 32 (3.13%)	3 / 60 (5.00%)	0 / 100 (0.00%)
occurrences (all)	1	3	0
Breast swelling			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 32 (9.38%)	10 / 60 (16.67%)	18 / 100 (18.00%)
occurrences (all)	5	14	21
Dysphonia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	4 / 100 (4.00%)
occurrences (all)	0	1	5
Interstitial lung disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	4 / 100 (4.00%)
occurrences (all)	0	2	4
Haemoptysis			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	4 / 100 (4.00%)
occurrences (all)	1	2	6
Epistaxis			

subjects affected / exposed	3 / 32 (9.38%)	4 / 60 (6.67%)	3 / 100 (3.00%)
occurrences (all)	3	4	3
Emphysema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	3 / 100 (3.00%)
occurrences (all)	1	2	4
Dyspnoea			
subjects affected / exposed	6 / 32 (18.75%)	12 / 60 (20.00%)	22 / 100 (22.00%)
occurrences (all)	6	14	23
Rhinitis allergic			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	3 / 100 (3.00%)
occurrences (all)	1	2	4
Pulmonary embolism			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	2 / 100 (2.00%)
occurrences (all)	2	4	2
Productive cough			
subjects affected / exposed	2 / 32 (6.25%)	5 / 60 (8.33%)	5 / 100 (5.00%)
occurrences (all)	2	7	5
Pneumonitis			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	4 / 100 (4.00%)
occurrences (all)	2	3	6
Pleurisy			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	2 / 100 (2.00%)
occurrences (all)	3	4	3
Pleural effusion			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	5 / 100 (5.00%)
occurrences (all)	2	2	6
Oropharyngeal pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	4 / 100 (4.00%)
occurrences (all)	0	0	4
Rhinorrhoea			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	4 / 100 (4.00%)
occurrences (all)	1	2	6
Psychiatric disorders			

Insomnia			
subjects affected / exposed	6 / 32 (18.75%)	11 / 60 (18.33%)	9 / 100 (9.00%)
occurrences (all)	6	11	10
Dysphoria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	6 / 100 (6.00%)
occurrences (all)	2	2	6
Confusional state			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	1 / 32 (3.13%)	3 / 60 (5.00%)	4 / 100 (4.00%)
occurrences (all)	1	3	4
Sleep disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	5 / 32 (15.63%)	7 / 60 (11.67%)	11 / 100 (11.00%)
occurrences (all)	5	7	17
Alanine aminotransferase increased			
subjects affected / exposed	3 / 32 (9.38%)	7 / 60 (11.67%)	16 / 100 (16.00%)
occurrences (all)	6	11	18
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	10 / 100 (10.00%)
occurrences (all)	3	5	13
Blood urine present			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	12 / 32 (37.50%)	22 / 60 (36.67%)	34 / 100 (34.00%)
occurrences (all)	44	57	70
Blood bilirubin increased			

subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	2 / 100 (2.00%)
occurrences (all)	2	6	2
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 32 (9.38%)	4 / 60 (6.67%)	8 / 100 (8.00%)
occurrences (all)	3	4	10
Blood albumin decreased			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	5 / 100 (5.00%)
occurrences (all)	2	2	8
Liver function test abnormal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	7 / 32 (21.88%)	12 / 60 (20.00%)	10 / 100 (10.00%)
occurrences (all)	13	18	32
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	6 / 100 (6.00%)
occurrences (all)	0	2	7
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences (all)	2	2	0
Liver function test increased			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	1	2	1
Lymphocyte count decreased			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	1 / 100 (1.00%)
occurrences (all)	5	6	1
Neutrophil count decreased			
subjects affected / exposed	3 / 32 (9.38%)	4 / 60 (6.67%)	3 / 100 (3.00%)
occurrences (all)	3	5	8
Platelet count decreased			

subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	6 / 100 (6.00%)
occurrences (all)	1	3	16
Procalcitonin increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	1	1	3
Weight decreased			
subjects affected / exposed	6 / 32 (18.75%)	10 / 60 (16.67%)	10 / 100 (10.00%)
occurrences (all)	6	10	12
Weight increased			
subjects affected / exposed	2 / 32 (6.25%)	5 / 60 (8.33%)	6 / 100 (6.00%)
occurrences (all)	2	5	6
White blood cell count decreased			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	2	4	1
Injury, poisoning and procedural complications			
Anastomotic ulcer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Face injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	4 / 100 (4.00%)
occurrences (all)	3	5	4
Head injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	3 / 100 (3.00%)
occurrences (all)	0	1	3
Pelvic fracture			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Sinus bradycardia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	4 / 100 (4.00%)
occurrences (all)	0	1	4
Palpitations			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	2 / 100 (2.00%)
occurrences (all)	2	4	2
Cardiac failure			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences (all)	2	2	0
Atrial fibrillation			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	1	1	2
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	4 / 32 (12.50%)	7 / 60 (11.67%)	12 / 100 (12.00%)
occurrences (all)	7	11	16
Paraesthesia			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	6 / 100 (6.00%)
occurrences (all)	2	3	6
Neuropathy peripheral			
subjects affected / exposed	3 / 32 (9.38%)	3 / 60 (5.00%)	2 / 100 (2.00%)
occurrences (all)	3	3	2
Hypoaesthesia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	1 / 32 (3.13%)	3 / 60 (5.00%)	11 / 100 (11.00%)
occurrences (all)	1	3	12
Dysgeusia			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	0 / 100 (0.00%)
occurrences (all)	2	3	0
Dysarthria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Taste disorder			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	1	1	2
Tremor			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	2 / 100 (2.00%)
occurrences (all)	0	2	4
Thrombocytopenia			
subjects affected / exposed	3 / 32 (9.38%)	3 / 60 (5.00%)	5 / 100 (5.00%)
occurrences (all)	3	3	12
Anaemia			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	12 / 100 (12.00%)
occurrences (all)	2	4	13
Leukopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1

Lymphopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	5 / 32 (15.63%)	7 / 60 (11.67%)	3 / 100 (3.00%)
occurrences (all)	5	7	3
Tinnitus			
subjects affected / exposed	1 / 32 (3.13%)	4 / 60 (6.67%)	3 / 100 (3.00%)
occurrences (all)	1	4	3
Vertigo			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	6 / 100 (6.00%)
occurrences (all)	0	1	8
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 32 (9.38%)	6 / 60 (10.00%)	4 / 100 (4.00%)
occurrences (all)	3	7	8
Abdominal discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	3 / 32 (9.38%)	8 / 60 (13.33%)	7 / 100 (7.00%)
occurrences (all)	3	8	8
Abnormal faeces			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	15 / 32 (46.88%)	28 / 60 (46.67%)	44 / 100 (44.00%)
occurrences (all)	19	38	64
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	2 / 100 (2.00%)
occurrences (all)	2	3	3
Dysphagia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences (all)	1	1	1
Dyspepsia			

subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	7 / 100 (7.00%)
occurrences (all)	2	4	7
Dry mouth			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	4 / 32 (12.50%)	9 / 60 (15.00%)	18 / 100 (18.00%)
occurrences (all)	7	14	22
Constipation			
subjects affected / exposed	3 / 32 (9.38%)	8 / 60 (13.33%)	12 / 100 (12.00%)
occurrences (all)	3	8	14
Vomiting			
subjects affected / exposed	6 / 32 (18.75%)	13 / 60 (21.67%)	27 / 100 (27.00%)
occurrences (all)	15	24	46
Stomatitis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	4 / 100 (4.00%)
occurrences (all)	3	3	4
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	3 / 100 (3.00%)
occurrences (all)	1	1	3
Eczema			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	3 / 100 (3.00%)
occurrences (all)	0	1	3
Pruritus			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	13 / 100 (13.00%)
occurrences (all)	5	7	17
Pruritus allergic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Rash			

subjects affected / exposed	3 / 32 (9.38%)	3 / 60 (5.00%)	10 / 100 (10.00%)
occurrences (all)	3	3	10
Rash maculo-papular			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Alopecia			
subjects affected / exposed	3 / 32 (9.38%)	4 / 60 (6.67%)	2 / 100 (2.00%)
occurrences (all)	3	4	2
Dermatitis acneiform			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	3 / 100 (3.00%)
occurrences (all)	2	2	5
Skin induration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	2	2	1
Stasis dermatitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	2	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 32 (6.25%)	9 / 60 (15.00%)	10 / 100 (10.00%)
occurrences (all)	2	9	14
Muscle spasms			

subjects affected / exposed	3 / 32 (9.38%)	6 / 60 (10.00%)	3 / 100 (3.00%)
occurrences (all)	3	7	4
Joint swelling			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Flank pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	7 / 32 (21.88%)	11 / 60 (18.33%)	22 / 100 (22.00%)
occurrences (all)	7	12	26
Muscular weakness			
subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	4 / 100 (4.00%)
occurrences (all)	2	3	4
Musculoskeletal chest pain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	7 / 100 (7.00%)
occurrences (all)	1	2	8
Musculoskeletal pain			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Pain in extremity			
subjects affected / exposed	3 / 32 (9.38%)	6 / 60 (10.00%)	12 / 100 (12.00%)
occurrences (all)	3	6	16
Neck pain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	5 / 100 (5.00%)
occurrences (all)	1	2	5
Myalgia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	7 / 100 (7.00%)
occurrences (all)	0	1	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	5 / 100 (5.00%)
occurrences (all)	0	0	5
Influenza			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	0 / 100 (0.00%)
occurrences (all)	1	1	0

Herpes zoster			
subjects affected / exposed	0 / 32 (0.00%)	1 / 60 (1.67%)	2 / 100 (2.00%)
occurrences (all)	0	1	2
Erysipelas			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences (all)	4	4	0
Epididymitis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences (all)	2	2	0
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 60 (3.33%)	7 / 100 (7.00%)
occurrences (all)	0	3	10
COVID-19			
subjects affected / exposed	3 / 32 (9.38%)	4 / 60 (6.67%)	3 / 100 (3.00%)
occurrences (all)	3	4	3
Nasopharyngitis			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	6 / 100 (6.00%)
occurrences (all)	3	6	8
Staphylococcal infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Pyuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	2 / 32 (6.25%)	4 / 60 (6.67%)	7 / 100 (7.00%)
occurrences (all)	2	4	12
Oral candidiasis			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	0 / 100 (0.00%)
occurrences (all)	1	2	0

Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	2 / 60 (3.33%)	1 / 100 (1.00%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	9 / 100 (9.00%)
occurrences (all)	5	5	11
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 60 (1.67%)	1 / 100 (1.00%)
occurrences (all)	1	1	1
Hypoalbuminaemia			
subjects affected / exposed	5 / 32 (15.63%)	8 / 60 (13.33%)	11 / 100 (11.00%)
occurrences (all)	8	11	18
Hypocalcaemia			
subjects affected / exposed	8 / 32 (25.00%)	11 / 60 (18.33%)	9 / 100 (9.00%)
occurrences (all)	9	14	10
Hypercalcaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	6 / 32 (18.75%)	14 / 60 (23.33%)	21 / 100 (21.00%)
occurrences (all)	8	17	26
Hypokalaemia			
subjects affected / exposed	4 / 32 (12.50%)	5 / 60 (8.33%)	5 / 100 (5.00%)
occurrences (all)	11	12	6
Hypomagnesaemia			
subjects affected / exposed	2 / 32 (6.25%)	2 / 60 (3.33%)	2 / 100 (2.00%)
occurrences (all)	3	3	2
Hypophosphataemia			
subjects affected / exposed	0 / 32 (0.00%)	3 / 60 (5.00%)	7 / 100 (7.00%)
occurrences (all)	0	4	13
Hypophagia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 60 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			

subjects affected / exposed	2 / 32 (6.25%)	3 / 60 (5.00%)	3 / 100 (3.00%)
occurrences (all)	6	7	4

Non-serious adverse events	All patients: On-treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	360 / 373 (96.51%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	19 / 373 (5.09%)		
occurrences (all)	23		
Embolism			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Hypertension			
subjects affected / exposed	13 / 373 (3.49%)		
occurrences (all)	14		
Deep vein thrombosis			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	9		
Superficial vein thrombosis			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	86 / 373 (23.06%)		
occurrences (all)	96		
Face oedema			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	10		
Chest discomfort			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	6		
Asthenia			

subjects affected / exposed	49 / 373 (13.14%)		
occurrences (all)	58		
Malaise			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	10		
Pyrexia			
subjects affected / exposed	49 / 373 (13.14%)		
occurrences (all)	66		
Peripheral swelling			
subjects affected / exposed	10 / 373 (2.68%)		
occurrences (all)	16		
Non-cardiac chest pain			
subjects affected / exposed	32 / 373 (8.58%)		
occurrences (all)	38		
Oedema			
subjects affected / exposed	8 / 373 (2.14%)		
occurrences (all)	9		
Oedema peripheral			
subjects affected / exposed	203 / 373 (54.42%)		
occurrences (all)	343		
Pain			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	9		
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	3 / 373 (0.80%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	3 / 373 (0.80%)		
occurrences (all)	3		
Breast swelling			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Breast pain			

subjects affected / exposed	3 / 373 (0.80%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	61 / 373 (16.35%)		
occurrences (all)	74		
Dysphonia			
subjects affected / exposed	11 / 373 (2.95%)		
occurrences (all)	12		
Interstitial lung disease			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
Hypoxia			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	6		
Haemoptysis			
subjects affected / exposed	16 / 373 (4.29%)		
occurrences (all)	18		
Epistaxis			
subjects affected / exposed	11 / 373 (2.95%)		
occurrences (all)	11		
Emphysema			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Dyspnoea exertional			
subjects affected / exposed	8 / 373 (2.14%)		
occurrences (all)	9		
Dyspnoea			
subjects affected / exposed	83 / 373 (22.25%)		
occurrences (all)	96		
Rhinitis allergic			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	6		
Pulmonary embolism			

subjects affected / exposed	15 / 373 (4.02%)		
occurrences (all)	16		
Productive cough			
subjects affected / exposed	19 / 373 (5.09%)		
occurrences (all)	21		
Pneumonitis			
subjects affected / exposed	11 / 373 (2.95%)		
occurrences (all)	15		
Pleurisy			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	7		
Pleural effusion			
subjects affected / exposed	17 / 373 (4.56%)		
occurrences (all)	24		
Oropharyngeal pain			
subjects affected / exposed	8 / 373 (2.14%)		
occurrences (all)	8		
Rhinorrhoea			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	11		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	34 / 373 (9.12%)		
occurrences (all)	35		
Dysphoria			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	12 / 373 (3.22%)		
occurrences (all)	12		
Confusional state			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Anxiety			
subjects affected / exposed	15 / 373 (4.02%)		
occurrences (all)	15		

Sleep disorder subjects affected / exposed occurrences (all)	5 / 373 (1.34%) 5		
Investigations Amylase increased subjects affected / exposed occurrences (all)	36 / 373 (9.65%) 49		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	53 / 373 (14.21%) 65		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	39 / 373 (10.46%) 49		
Blood urine present subjects affected / exposed occurrences (all)	1 / 373 (0.27%) 1		
Blood creatinine increased subjects affected / exposed occurrences (all)	103 / 373 (27.61%) 238		
Blood bilirubin increased subjects affected / exposed occurrences (all)	13 / 373 (3.49%) 24		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	25 / 373 (6.70%) 28		
Blood albumin decreased subjects affected / exposed occurrences (all)	13 / 373 (3.49%) 17		
Liver function test abnormal subjects affected / exposed occurrences (all)	2 / 373 (0.54%) 2		
Lipase increased subjects affected / exposed occurrences (all)	37 / 373 (9.92%) 71		
Gamma-glutamyltransferase increased			

subjects affected / exposed	24 / 373 (6.43%)			
occurrences (all)	30			
Eastern Cooperative Oncology Group performance status worsened				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences (all)	1			
C-reactive protein increased				
subjects affected / exposed	9 / 373 (2.41%)			
occurrences (all)	10			
Liver function test increased				
subjects affected / exposed	4 / 373 (1.07%)			
occurrences (all)	4			
Lymphocyte count decreased				
subjects affected / exposed	5 / 373 (1.34%)			
occurrences (all)	9			
Neutrophil count decreased				
subjects affected / exposed	14 / 373 (3.75%)			
occurrences (all)	21			
Platelet count decreased				
subjects affected / exposed	17 / 373 (4.56%)			
occurrences (all)	34			
Procalcitonin increased				
subjects affected / exposed	1 / 373 (0.27%)			
occurrences (all)	1			
Protein total decreased				
subjects affected / exposed	3 / 373 (0.80%)			
occurrences (all)	4			
Weight decreased				
subjects affected / exposed	41 / 373 (10.99%)			
occurrences (all)	44			
Weight increased				
subjects affected / exposed	21 / 373 (5.63%)			
occurrences (all)	22			
White blood cell count decreased				
subjects affected / exposed	8 / 373 (2.14%)			
occurrences (all)	13			

Injury, poisoning and procedural complications			
Anastomotic ulcer			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Face injury			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	11 / 373 (2.95%)		
occurrences (all)	14		
Head injury			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences (all)	4		
Pelvic fracture			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
Spinal compression fracture			
subjects affected / exposed	3 / 373 (0.80%)		
occurrences (all)	3		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	6		
Sinus bradycardia			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Palpitations			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	11		
Cardiac failure			
subjects affected / exposed	3 / 373 (0.80%)		
occurrences (all)	3		
Atrial fibrillation			

subjects affected / exposed	8 / 373 (2.14%)		
occurrences (all)	9		
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	34 / 373 (9.12%)		
occurrences (all)	43		
Paraesthesia			
subjects affected / exposed	15 / 373 (4.02%)		
occurrences (all)	16		
Neuropathy peripheral			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	6		
Hypoaesthesia			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	30 / 373 (8.04%)		
occurrences (all)	34		
Dysgeusia			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	6		
Dysarthria			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
Somnolence			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Syncope			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Taste disorder			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		

Tremor subjects affected / exposed occurrences (all)	6 / 373 (1.61%) 7		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all)	 9 / 373 (2.41%) 13 9 / 373 (2.41%) 16 35 / 373 (9.38%) 43 6 / 373 (1.61%) 7 5 / 373 (1.34%) 5		
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	 14 / 373 (3.75%) 14 8 / 373 (2.14%) 8 15 / 373 (4.02%) 17		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain upper	 23 / 373 (6.17%) 30 5 / 373 (1.34%) 5		

subjects affected / exposed	27 / 373 (7.24%)		
occurrences (all)	30		
Abnormal faeces			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	170 / 373 (45.58%)		
occurrences (all)	223		
Gastrooesophageal reflux disease			
subjects affected / exposed	12 / 373 (3.22%)		
occurrences (all)	13		
Dysphagia			
subjects affected / exposed	17 / 373 (4.56%)		
occurrences (all)	18		
Dyspepsia			
subjects affected / exposed	26 / 373 (6.97%)		
occurrences (all)	27		
Dry mouth			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	70 / 373 (18.77%)		
occurrences (all)	92		
Constipation			
subjects affected / exposed	69 / 373 (18.50%)		
occurrences (all)	74		
Vomiting			
subjects affected / exposed	102 / 373 (27.35%)		
occurrences (all)	156		
Stomatitis			
subjects affected / exposed	11 / 373 (2.95%)		
occurrences (all)	12		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		

Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	19 / 373 (5.09%)		
occurrences (all)	21		
Eczema			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	35 / 373 (9.38%)		
occurrences (all)	43		
Pruritus allergic			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	24 / 373 (6.43%)		
occurrences (all)	25		
Rash maculo-papular			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	6		
Alopecia			
subjects affected / exposed	10 / 373 (2.68%)		
occurrences (all)	10		
Dermatitis acneiform			
subjects affected / exposed	7 / 373 (1.88%)		
occurrences (all)	9		
Skin induration			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
Skin lesion			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences (all)	4		
Stasis dermatitis			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	3 / 373 (0.80%)		
occurrences (all)	3		
Dysuria			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences (all)	5		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	7 / 373 (1.88%)		
occurrences (all)	8		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	39 / 373 (10.46%)		
occurrences (all)	49		
Muscle spasms			
subjects affected / exposed	26 / 373 (6.97%)		
occurrences (all)	29		
Joint swelling			
subjects affected / exposed	6 / 373 (1.61%)		
occurrences (all)	6		
Flank pain			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	63 / 373 (16.89%)		
occurrences (all)	68		
Muscular weakness			
subjects affected / exposed	10 / 373 (2.68%)		
occurrences (all)	10		
Musculoskeletal chest pain			
subjects affected / exposed	18 / 373 (4.83%)		
occurrences (all)	19		
Musculoskeletal pain			
subjects affected / exposed	9 / 373 (2.41%)		
occurrences (all)	10		
Pain in extremity			

subjects affected / exposed	31 / 373 (8.31%)		
occurrences (all)	37		
Neck pain			
subjects affected / exposed	8 / 373 (2.14%)		
occurrences (all)	8		
Myalgia			
subjects affected / exposed	19 / 373 (5.09%)		
occurrences (all)	19		
Infections and infestations			
Bronchitis			
subjects affected / exposed	10 / 373 (2.68%)		
occurrences (all)	11		
Influenza			
subjects affected / exposed	5 / 373 (1.34%)		
occurrences (all)	5		
Herpes zoster			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences (all)	4		
Erysipelas			
subjects affected / exposed	4 / 373 (1.07%)		
occurrences (all)	6		
Epididymitis			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
Cellulitis			
subjects affected / exposed	13 / 373 (3.49%)		
occurrences (all)	17		
COVID-19			
subjects affected / exposed	7 / 373 (1.88%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	24 / 373 (6.43%)		
occurrences (all)	31		
Staphylococcal infection			
subjects affected / exposed	1 / 373 (0.27%)		
occurrences (all)	1		

Sepsis subjects affected / exposed occurrences (all)	3 / 373 (0.80%) 3		
Rhinitis subjects affected / exposed occurrences (all)	2 / 373 (0.54%) 2		
Pyuria subjects affected / exposed occurrences (all)	1 / 373 (0.27%) 1		
Pneumonia subjects affected / exposed occurrences (all)	27 / 373 (7.24%) 35		
Oral candidiasis subjects affected / exposed occurrences (all)	5 / 373 (1.34%) 5		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 373 (1.34%) 5		
Urinary tract infection subjects affected / exposed occurrences (all)	13 / 373 (3.49%) 19		
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	9 / 373 (2.41%) 10		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	38 / 373 (10.19%) 55		
Hypocalcaemia subjects affected / exposed occurrences (all)	23 / 373 (6.17%) 28		
Hypercalcaemia subjects affected / exposed occurrences (all)	6 / 373 (1.61%) 6		
Decreased appetite			

subjects affected / exposed	80 / 373 (21.45%)		
occurrences (all)	90		
Hypokalaemia			
subjects affected / exposed	23 / 373 (6.17%)		
occurrences (all)	35		
Hypomagnesaemia			
subjects affected / exposed	7 / 373 (1.88%)		
occurrences (all)	8		
Hypophosphataemia			
subjects affected / exposed	20 / 373 (5.36%)		
occurrences (all)	30		
Hypophagia			
subjects affected / exposed	2 / 373 (0.54%)		
occurrences (all)	2		
Hyponatraemia			
subjects affected / exposed	15 / 373 (4.02%)		
occurrences (all)	21		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2015	Assessment of ALK rearrangement determined with a validated test is considered as part of the non-squamous NSCLC subject's standard of care and therefore ALK-negative rearrangement status was required for subjects with non-squamous NSCLC in order to be enrolled in the study. The inclusion and exclusion criterion was amended accordingly.
11 September 2015	A new cohort (Cohort 4) was implemented to enroll subjects with MET mutations, irrespective of MET amplification status. For subjects already enrolled in the study prior to the implementation of this amendment, the MET mutation status was to be determined retrospectively, however these subjects remained in the cohort to which they were initially enrolled. Photosensitization: precautionary measures against ultraviolet exposure were included. Dose modification guidelines for hepatotoxicity were modified in regard to discontinuing study medication(s) with concurrent elevation of ALT and/or AST > 3 × ULN and total bilirubin > 2 × ULN with ALP < 2 × ULN, in the absence of signs of cholestasis, hemolysis, and alternative causes of the liver injury. Specific work-up guidelines for potential drug-induced liver injury (DILI) cases were added to the protocol. The dose modification rules as well as the follow-up evaluations for hepatic toxicities were also updated accordingly. Clinical PK data were updated with the recent data from study CINC280X2102 and CIN280X1101 that identified CMN288 as a major metabolite of capmatinib. Characterization of CMN288 metabolite was added in the PK objective.
28 July 2016	To further investigate and better characterize the optimal GCN as predictor of response to capmatinib. The following 2 subcohorts were implemented within Cohort 1 (Cohort 1: Subjects with a MET GCN of ≥ 6): • Subcohort 1a (referred to as Cohort 1a in the CSR): Subjects with a MET GCN of ≥ 10, or • Subcohort 1b (referred to as Cohort 1b in the CSR): Subjects with a MET GCN of ≥ 6 and < 10 Each of the two subcohorts were to be tested independently. Restrictions on the use of PPIs as concomitant medications were removed.
17 November 2016	A new cohort (Cohort 5) was added to enroll treatment-naïve subjects with MET dysregulation: Cohort 5: Treatment-naïve subjects with MET dysregulation: •Subcohort 5a (referred to as Cohort 5a in the CSR): Subjects with a MET GCN ≥ 10 (without MET mutations) •Subcohort 5b (referred to as Cohort 5b in the CSR): Subjects with MET mutations regardless of MET GCN
13 February 2018	A new expansion Cohort 6 was added for enrollment of additional 30 subjects approximately with advanced NSCLC pretreated with one prior line of systemic therapy harboring either MET amplification (GCN ≥ 10) or MET mutations (irrespective of MET GCN). Exclusion criteria, the list of prohibited medications, the list of medications to be used with caution and the criteria for dose modifications were updated based on the latest capmatinib clinical data per IB, edition 9.

28 February 2019	A new expansion Cohort 7 was added for the enrollment of approximately 27 treatment-naïve subjects with advanced NSCLC harboring MET exon 14 skipping mutations (regardless of MET GCN). Close the recruitment of NSCLC subjects with GCN ≥ 10 in Cohort 5a and Cohort 6. Therefore, as of 25-Jan-2019, pre-screening for MET GCN ≥ 10 NSCLC subjects and central FISH (Fluorescence In Situ Hybridization) testing for MET GCN eligibility was discontinued. Cycle 1 Day 1 blood collection increased to 3x10 mL from 2x10 mL. Implement an additional on-treatment blood sample collection (2 x 10 mL) at C3D1

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 9999 as data points in this record are not an accurate representation of the clinical trial results.

Notes: