Clinical trial results:
A Multicenter, Open-Label Phase 1b/2 Trial of Lenvatinib (E7080) Plus Pembrolizumab in Subjects With Selected Solid Tumors

Summary

EudraCT number	2017-000300-26
Trial protocol	ES NO
Global end of trial date	11 July 2022

Results information

Result version number	v1 (current)
This version publication date	09 July 2023
First version publication date	09 July 2023

Trial information

Trial identification

Sponsor protocol code	E7080-A001-111

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02501096
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Ltd.,
Sponsor organisation address	European Knowledge Centre Mosquito Way, Hatfield, Hertfordshire, United Kingdom, AL10 9SN
Public contact	EMEA Medical Information, Eisai Europe Ltd.,, +44 (0)208 600 1400, EUMedInfo@eisai.net
Scientific contact	EMEA Medical Information, Eisai Europe Ltd.,, +44 (0)208 600 1400, EUMedInfo@eisai.net

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	11 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was an open-label Phase 1b/2 trial of lenvatinib (E7080) plus pembrolizumab in subjects with selected solid tumors. Phase 1b was to determine and confirm the maximum tolerated dose (MTD) for lenvatinib in combination with 200 milligrams (mg) (intravenous [IV], every 3 weeks [Q3W]) pembrolizumab in subjects with selected solid tumors (that is, non-small cell lung cancer, renal cell carcinoma, endometrial carcinoma, urothelial carcinoma, squamous cell carcinoma of the head and neck, Leiomyosarcoma or melanoma). Phase 2 (Expansion) was to evaluate the safety and efficacy of the combination in 7 cohorts at the MTD from Phase 1b (Phase 1b/2: lenvatinib 20 milligram per day (mg/day) orally + pembrolizumab 200 mg Q3W, IV).

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following: - Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008) - International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use - Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312 - European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states. - Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 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	United States: 320
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Spain: 31
Worldwide total number of subjects	357
EEA total number of subjects	37

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)	174
From 65 to 84 years	180
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 62 investigative sites in the United States, Spain and Norway from 22 July 2015 to 11 July 2022.

Pre-assignment

Screening details:

357 subjects were enrolled/treated.Of which 13 subjects enrolled in Phase 1b(3 subjects received lenvatinib 24mg and 10 subjects received lenvatinib 20mg with pembrolizumab);344 from Phase 2 received lenvatinib 20mg+pembrolizumab 200mg.As planned,Phase 1b/2 data for subjects in lenvatinib 20mg+pembrolizumab 200mg was combined/presented together.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC

Arm description:

Subjects with Renal Cell Carcinoma (RCC) received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until disease progression (PD), development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC

Arm description:

Subject with Non-small Cell Lung Cancer (NSCLC) received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC

Arm description:

Subjects with Endometrial Carcinoma (EC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC

Arm description:

Subjects with RCC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma

Arm description:

Subjects with Melanoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC

Arm description:

Subjects with NSCLC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:

	HNSCC

Arm description:

Subjects with Squamous Cell Carcinoma of Head and Neck (HNSCC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC

Arm description:

Subjects with Urothelial Carcinoma (UC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Arm title	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma

Arm description:

Subject with Leiomyosarcoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Arm type	Experimental

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475/KEYTRUDA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab administered as an IV infusion, Q3W in a 21-day treatment cycle.

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib administered orally, once a day (with or without food) in 21-day cycles at approximately the same time each day.

Number of subjects in period 1	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC
Started	2	1	124
Phase 1b subjects who received Len 20 mg	0	0	2
Phase 2 subjects who received Len 20 mg	0	0	122
Completed	0	0	0
Not completed	2	1	124
Death	1	1	88
Survival follow-up discontinued by sponsor	-	-	29
Withdrawal of consent from study	1	-	7
Lost to follow-up	-	-	-

Number of subjects in period 1	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Started	145	21	21
Phase 1b subjects who received Len 20 mg	6	1	1
Phase 2 subjects who received Len 20 mg	139	20	20
Completed	0	0	0
Not completed	145	21	21
Death	74	15	16
Survival follow-up discontinued by sponsor	58	3	2
Withdrawal of consent from study	13	2	2
Lost to follow-up	-	1	1

Number of subjects in period 1	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma
Started	22	20	1
Phase 1b subjects who received Len 20 mg	0	0	0
Phase 2 subjects who received Len 20 mg	22	20	1
Completed	0	0	0
Not completed	22	20	1
Death	15	16	1
Survival follow-up discontinued by sponsor	2	1	-
Withdrawal of consent from study	2	3	-
Lost to follow-up	3	-	-

Baseline characteristics

Reporting groups

Reporting group title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC

Reporting group description:

Subjects with Renal Cell Carcinoma (RCC) received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until disease progression (PD), development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC

Reporting group description:

Subject with Non-small Cell Lung Cancer (NSCLC) received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC

Reporting group description:

Subjects with Endometrial Carcinoma (EC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC

Reporting group description:

Subjects with RCC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma

Reporting group description:

Subjects with Melanoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC

Reporting group description:

Subjects with NSCLC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC

Reporting group description:

Subjects with Squamous Cell Carcinoma of Head and Neck (HNSCC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC

Reporting group description:

Subjects with Urothelial Carcinoma (UC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma

Reporting group description:

Subject with Leiomyosarcoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group values	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC
Number of subjects	2	1	124
Age Categorical Units: subjects			
<65 years	0	0	47
>=65 years	2	1	77
Gender Categorical Units: subjects			
Female	0	1	124
Male	2	0	0
Race Units: Subjects			
White	2	1	108
Black or African American	0	0	7
Asian	0	0	5
American Indian or Alaskan Native	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	1
Other	0	0	2
Missing	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	3
Non Hispanic or Latino	1	1	121

Reporting group values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Number of subjects	145	21	21
Age Categorical Units: subjects			
<65 years	88	16	9
>=65 years	57	5	12
Gender Categorical Units: subjects			
Female	32	4	10
Male	113	17	11
Race Units: Subjects			
White	125	19	18
Black or African American	6	0	3
Asian	3	0	0

American Indian or Alaskan Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	8	1	0
Missing	3	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	17	2	0
Non Hispanic or Latino	128	19	21

Reporting group values	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma
Number of subjects	22	20	1
Age Categorical Units: subjects			
<65 years	9	4	1
>=65 years	13	16	0
Gender Categorical Units: subjects			
Female	4	6	1
Male	18	14	0
Race Units: Subjects			
White	20	19	0
Black or African American	2	0	1
Asian	0	0	0
American Indian or Alaskan Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	0	1	0
Missing	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	0
Non Hispanic or Latino	21	18	1

Reporting group values	Total		
Number of subjects	357		
Age Categorical Units: subjects			
<65 years	174		
>=65 years	183		
Gender Categorical Units: subjects			
Female	182		
Male	175		
Race Units: Subjects			
White	312		
Black or African American	19		
Asian	8		

American Indian or Alaskan Native	1		
Native Hawaiian or Other Pacific Islander	1		
Other	12		
Missing	4		
Ethnicity Units: Subjects			
Hispanic or Latino	26		
Non Hispanic or Latino	331		

End points reporting groups

Reporting group title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC

Reporting group description:

Subjects with Renal Cell Carcinoma (RCC) received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until disease progression (PD), development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC

Reporting group description:

Subject with Non-small Cell Lung Cancer (NSCLC) received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC

Reporting group description:

Subjects with Endometrial Carcinoma (EC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC

Reporting group description:

Subjects with RCC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma

Reporting group description:

Subjects with Melanoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC

Reporting group description:

Subjects with NSCLC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC

Reporting group description:

Subjects with Squamous Cell Carcinoma of Head and Neck (HNSCC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC

Reporting group description:

Subjects with Urothelial Carcinoma (UC) received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:

	Leiomyosarcoma

Reporting group description:

Subject with Leiomyosarcoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Subject analysis set title	Phase 1b, Lenvatinib 20 mg/day + Pembrolizumab 200 mg: NSCLC
Subject analysis set type	Safety analysis

Subject analysis set description:

Subject with NSCLC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Subject analysis set title	Phase 1b, Lenvatinib 20 mg/day + Pembrolizumab 200 mg: RCC
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with RCC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Subject analysis set title	Phase 1b, Lenvatinib 20 mg/day + Pembrolizumab 200 mg: EC
Subject analysis set type	Safety analysis

Subject analysis set description:

Subject with NSCLC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Subject analysis set title	Phase 1b, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma
Subject analysis set type	Safety analysis

Subject analysis set description:

Subject with Melanoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Subject analysis set title	Phase 1b: All Subjects
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects with selected solid tumors (RCC, EC, NSCLC and Melanoma) received lenvatinib 24 or 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subjects choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Primary: Phase 1b: Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of Lenvatinib

End point title	Phase 1b: Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D) of Lenvatinib[1]

End point description:

MTD:confirmed if no more than 3 subjects experience dose-limiting toxicities(DLTs)during first 3 weeks(Cycle 1) of treatment.If MTD not confirmed at dose level,then enrollment proceeded to next lower dose level.Sponsor reviewed data to determine RP2D.DLT from following:hematological/nonhematological toxicities considered to be at least possibly related to Lenvatinib/pembrolizumab occurring during Cycle 1.Failure to administer greater than or equal to(>=)75 percent(%) of planned dosage of lenvatinib as result of treatment-related toxicity during Cycle 1.Who discontinue treatment due to treatment-related toxicity.Greater than 2 week delay in starting Cycle 2 because of treatment-related toxicity,even if toxicity does not meet DLT criteria.Toxicity evaluated as per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03(NCI CTCAE v 4.03).MTD analysis included all subjects who completed Cycle 1 of treatment in Phase 1b or

End point type	Primary

End point timeframe:

Cycle 1 (21 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Phase 1b: All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: milligram (mg)				
number (not applicable)				
MTD	20			
RP2D	20			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) Based on Immune-related Response Evaluation Criteria in Solid Tumors (irRECIST) at Week 24

End point title	Objective Response Rate (ORR) Based on Immune-related Response Evaluation Criteria in Solid Tumors (irRECIST) at Week 24[2][3]

End point description:

ORR was defined as the percentage of subjects whose best overall response (BOR) was immune related complete response (irCR) or immune related partial response (irPR) based on investigator assessment according to response evaluation criteria in solid tumors to (irRECIST) version 1.1. irCR was defined as disappearance of all target lesions. Any pathological lymph nodes (target or non-target) had to be reduced in short axis to less than (<) 10 millimeter (mm). irPR was defined as at least a 30% decrease in sum of diameters of target lesions, taking as reference the baseline sum of diameters. The full analysis set (FAS) included all subjects who entered the study treatment period. Here, 99999 indicate that number and 95% confidence interval (CI) could not be estimated as insufficient number of subjects were available for analysis in this arm.

End point type	Primary

End point timeframe:

Week 24

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	145	21	21
Units: percentage of subjects				
number (confidence interval 95%)	39.5 (30.9 to	56.6 (48.1 to	47.6 (25.7 to	23.8 (8.2 to

	48.7)	64.8)	70.2)	47.2)

End point values	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: percentage of subjects				
number (confidence interval 95%)	31.8 (13.9 to 54.9)	25.0 (8.7 to 49.1)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b: Number of Subjects With Dose Limiting Toxicities (DLTs) of Lenvatinib

End point title	Phase 1b: Number of Subjects With Dose Limiting Toxicities (DLTs) of Lenvatinib[4][5]

End point description:

A DLT was defined as any of the following: any of the hematological or nonhematological toxicities considered to be at least possibly related to lenvatinib and/or pembrolizumab occurring during Cycle 1. Failure to administer >=75% of the planned dosage of lenvatinib as a result of treatment-related toxicity during Cycle 1. Subjects who discontinue treatment due to treatment-related toxicity. Greater than 2 week delay in starting Cycle 2 because of a treatment-related toxicity, even if the toxicity does not meet DLT criteria. Toxicity was evaluated as per NCI CTCAE v 4.03. The MTD analysis set included all subjects who completed Cycle 1 of treatment in Phase 1b or discontinued early due to DLT.

End point type	Primary

End point timeframe:

Cycle 1 (21 days)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b of the study only.

End point values	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b, Lenvatinib 20 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b, Lenvatinib 20 mg/day + Pembrolizumab 200 mg: RCC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	2	1	1	6
Units: subjects	1	1	0	0

End point values	Phase 1b, Lenvatinib 20 mg/day + Pembrolizumab 200 mg: EC	Phase 1b, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	1		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

TEAE:adverse event(AE) emerged during treatment, having been absent at pretreatment or reemerged during treatment, present at pretreatment but stopped before treatment or worsened in severity during treatment relative to pretreatment state, when AE is continuous. AE:any untoward medical occurrence in subject administered an investigational product.TEAEs were based on subjects laboratory tests, regular measurement of vital signs, echocardiograms/multigated acquisition scans to assess left ventricular ejection fraction and electrocardiograms parameter values.TESAE: any untoward medical occurrence that at any dose: resulted in death; life threatening condition; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; a congenital anomaly/birth defect or was medically important due to reasons other than above criteria. Safety analysis set included all subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From date of first dose up to 30 days after the last dose of study drug (Up to 74 months)

End point values	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	124	145
Units: subjects				
TEAEs	2	1	124	145
TESAEs	1	1	73	81

End point values	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	21	22	20
Units: subjects				
TEAEs	21	21	22	20
TESAEs	12	15	12	17

End point values	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: subjects				
TEAEs	1			
TESAEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) Based on irRECIST Version 1.1

End point title	Objective Response Rate (ORR) Based on irRECIST Version

End point description:

ORR was defined as the percentage of subjects whose BOR was irCR or irPR according to irRECIST version 1.1. irCR was defined as disappearance of all target lesions. Any pathological lymph nodes (target or non-target) had to be reduced in short axis to <10 mm. irPR was defined as at least a 30% decrease in sum of diameters of target lesions, taking as reference the baseline sum of diameters. The FAS included all subjects who entered the study treatment period. Here, 99999 indicate that number and 95% CI could not be estimated as insufficient number of subjects were available for analysis in this arm.

End point type	Secondary

End point timeframe:

From date of first dose of study drug administration until immune related PD (irPD), development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor (up to 73 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	145	21	21
Units: percentage of subjects				
number (confidence interval 95%)	40.3 (31.6 to 49.5)	63.4 (55.1 to 71.3)	47.6 (25.7 to 70.2)	23.8 (8.2 to 47.2)

End point values	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: percentage of subjects				
number (confidence interval 95%)	40.9 (20.7 to 63.6)	25.0 (8.7 to 49.1)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) Based on irRECIST Version 1.1

End point title	Progression-free Survival (PFS) Based on irRECIST Version

End point description:

PFS was defined as the time from the first dose date to the date of irPD or date of death (whichever occurred first) according to irRECIST version 1.1. irPD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this included the baseline sum if that was the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions was also considered progression). The FAS included all subjects who entered the study treatment period. Here “99999” indicate that 95% CI could not be estimated as insufficient number of subjects were available for analysis in this arm.

End point type	Secondary

End point timeframe:

From date of first dose of study drug administration to date of irPD or date of death, whichever occurred first (up to 73 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	145	21	21
Units: months				
median (confidence interval 95%)	7.5 (5.3 to 9.7)	14.1 (11.6 to 18.4)	5.5 (2.6 to 15.8)	5.4 (2.3 to 7.4)

End point values	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: months				
median (confidence interval 95%)	4.4 (4.0 to 9.8)	5.4 (1.3 to 42.3)	1.35 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) Based on irRECIST Version 1.1

End point title	Disease Control Rate (DCR) Based on irRECIST Version 1.1[8]

End point description:

DCR: percentage of subjects with a confirmed irCR, irPR, or irSD (duration of irSD greater than or equal to [>=] 5 weeks). DCR was assessed on irRECIST v1.1.irCR:disappearance of all target lesions. All pathological lymph nodes (whether target or non-target)must have reduction in their short axis to <10 mm.irPR: at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference baseline sum of longest diameter. irSD: neither sufficient shrinkage to qualify for irPR nor sufficient increase to qualify for irPD, taking as reference smallest sum diameters while on study.irPD: at least a 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study(this includes baseline sum if that is the smallest on study). The FAS included all subjects who entered the study treatment period. Here "99999" indicated that Number and 95% CI could not be estimated as insufficient number of subjects were available for analysis in this arm.

End point type	Secondary

End point timeframe:

From first dose of the study drug until irPD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor (up to 73 months)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	145	21	21
Units: percentage of subjects				
number (confidence interval 95%)	84.7 (77.1 to 90.5)	93.8 (88.5 to 97.1)	81.0 (58.1 to 94.6)	76.2 (52.8 to 91.8)

End point values	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: percentage of subjects				
number (confidence interval 95%)	90.9 (70.8 to 98.9)	70.0 (45.7 to 88.1)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[9]

End point description:

OS was defined as the time from the first dose date to the date of death from any cause. The FAS included all subjects who entered the study treatment period. Here "99999" indicated that 95% CI could not be estimated as insufficient number of subjects were available for analysis in this arm.

End point type	Secondary

End point timeframe:

From the first dose until death from any cause, up to 73 months

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	145	21	21
Units: months				
median (confidence interval 95%)	19.9 (16.2 to 25.9)	32.2 (29.8 to 55.8)	25.4 (8.6 to 39.5)	11.4 (3.6 to 23.3)

End point values	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: months				
median (confidence interval 95%)	16.2 (8.6 to 31.8)	6.1 (2.4 to 30.1)	16.56 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) Based on irRECIST Version 1.1

End point title	Clinical Benefit Rate (CBR) Based on irRECIST Version 1.1[10]

End point description:

CBR: percentage of subjects with BOR of irCR or irPR or irdurable stable disease (irdSD) (duration of irSD >=23 weeks) [irCR + irPR + irdSD] based on irRECIST v1.1. irCR: disappearance of all target lesions. All pathological lymph nodes (whether target or non-target) must have reduction in their short axis to <10 mm. irPR: at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference baseline sum of longest diameter. irSD: neither sufficient shrinkage to qualify for irPR nor sufficient increase to qualify for irPD, taking as reference smallest sum diameters while on study. irPD: at least a 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study (this includes baseline sum if that is the smallest on study). The FAS included all subjects who entered the study treatment period. Here "99999": Number and 95% CI could not be estimated as insufficient number of subjects were available for analysis in this arm.

End point type	Secondary

End point timeframe:

From first dose date until irPD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor (up to 73 months)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	124	145	21	21
Units: percentage of subjects				
number (confidence interval 95%)	58.9 (49.7 to 67.6)	80.0 (72.6 to 86.2)	61.9 (38.4 to 81.9)	57.1 (34.0 to 78.2)

End point values	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: percentage of subjects				
number (confidence interval 95%)	45.5 (24.4 to 67.8)	40.0 (19.1 to 63.9)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Durable Stable Disease Rate (DSDR) Based on irRECIST Version 1.1

End point title	Durable Stable Disease Rate (DSDR) Based on irRECIST Version 1.1[11]

End point description:

Durable SD rate is defined as the percentage of subjects whose observed BOR is irSD and the duration of irSD is >=23 weeks based on irRECIST v1.1. As planned, data for this endpoint dSD rate (where SD>=23 weeks) was not analyzed and collected separately but was included and analyzed in endpoint CBR (irCR+irPR+[irSD duration >=23 weeks]).

End point type	Secondary

End point timeframe:

From first dose date until irPD, development of unacceptable toxicity, participant choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor (up to 73 months)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[12]	0[13]	0[14]	0[15]
Units: percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[12] - No, subject was analyzed for this arm.

[13] - No, subject was analyzed for this arm.

[14] - No, subject was analyzed for this arm.

[15] - No, subject was analyzed for this arm.

End point values	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[16]	0[17]	0[18]	
Units: percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[16] - No, subject was analyzed for this arm.

[17] - No, subject was analyzed for this arm.

[18] - No, subject was analyzed for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (DOR) Based on irRECIST Version 1.1

End point title	Duration of Objective Response (DOR) Based on irRECIST Version 1.1[19]

End point description:

DOR:time from date of first observation of response(irPR or irCR)to date of first observation of progression based on irRECIST 1.1,or date of death, whatever the cause. irCR:disappearance of all target and non-target lesions. All pathological (whether target or non-target) must have reduction in their short axis <10 mm. irPR:at least 30% decrease in SOD of target lesions, taking as reference baseline sum diameters. irPD was defined as at least 20% increase(including an absolute increase of at least 5 mm)in SOD of target lesions,taking as reference smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions.The FAS included all subjects who entered the study treatment period.Here "number of subjects analyzed" signifies subjects who had irCR or irPR and '99999' indicated that median and/or upper limit could not be estimated as insufficient number of subjects were available for analysis.

End point type	Secondary

End point timeframe:

First documentation of irCR or irPR until f first documentation of progression or death up to 73 months

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be analyzed for Phase 1b and 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	92	10	5
Units: months				
median (confidence interval 95%)	99999 (8.5 to 99999)	16.6 (9.7 to 18.4)	12.5 (2.7 to 28.6)	14.5 (2.4 to 99999)

End point values	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	5	0[20]	
Units: months				

median (confidence interval 95%)	7.1 (2.2 to 16.8)	41.0 (4.6 to 99999)	(to)	

Notes:

[20] - Here, "N" is zero as there were no events of CR or PR in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Plasma Concentrations of Lenvatinib

End point title	Phase 1b: Plasma Concentrations of Lenvatinib[21]

End point description:

Lenvatinib was quantified using validated high-performance liquid chromatography-tandem mass spectroscopy (LCMS/MS) method. The Pharmacokinetic (PK) analysis set included all subjects who had received at least 1 dose of lenvatinib and had evaluable concentration data. Here number analyzed "n" signifies number of subjects who were evaluable for given time points. Here “99999” indicated that standard deviation could not be calculated because only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1: 0.5-4 hours and 6-10 hours post dose; Cycle 1 Day 15: predose, 0.5-4 hours and 6-10 hours post dose, Cycle 2 Day 1: predose, 2-12 hour postdose and Cycles 3,4,5,6 Day 1 predose (Cycle length =21 days)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 1b of the study only.

End point values	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: mcg/L				
arithmetic mean (standard deviation)				
Cycle 1 Day 1: 0.5-4 hour (n=2,1)	102.5 (± 136.44)	198.0 (± 99999)		
Cycle 1 Day 1: 6-10 hour (n=2,0)	210.5 (± 65.76)	99999 (± 99999)		
Cycle 1 Day 15: Predose (n=1,1)	53.9 (± 99999)	1.8 (± 99999)		
Cycle 1 Day 15: 0.5-4 hour (n=1,1)	78.4 (± 99999)	2.6 (± 99999)		
Cycle 1 Day 15: 6-10 hour (n=1,1)	366.0 (± 99999)	424.0 (± 99999)		
Cycle 2 Day 1: Predose (n=2,1)	35.4 (± 13.08)	364.0 (± 99999)		
Cycle 2 Day 1: 2-12 hour (n=2,1)	491.0 (± 247.49)	374.0 (± 99999)		
Cycle 3 Day 1: Predose (n=2,1)	23.3 (± 31.92)	118.0 (± 99999)		
Cycle 4 Day 1: Predose (n=2,1)	28.0 (± 13.93)	176.0 (± 99999)		
Cycle 5 Day 1: Predose (n=2,1)	19.9 (± 14.91)	2.5 (± 99999)		

Cycle 6 Day 1: Predose (n=2,1)	44.4 (± 42.64)	210.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Lenvatinib

End point title	Plasma Concentrations of Lenvatinib[22]

End point description:

Lenvatinib was quantified using validated LCMS/MS method. The PK analysis set included all subjects who had received at least 1 dose of lenvatinib and had evaluable concentration data. Here, overall number of subjects analyzed signifies subjects who were evaluable for this outcome measure and number analyzed "n" signifies number subjects who were evaluable for given time points. Here “99999” indicated that standard deviation could not be calculated because only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1: 0.5-4 hours and 6-10 hours post dose; Cycle 1 Day 15: predose, 0.5-4 hours and 6-10 hours post dose, Cycle 2 Day 1: predose, 2-12 hour postdose and Cycles 3,4,5,6 Day 1 predose (Cycle length =21 days)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analyzed for Phase 2 of the study only.

End point values	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	122	138	20	20
Units: mcg/L				
arithmetic mean (standard deviation)				
Cycle 1 Day 1:0.5-4 hour(n=122,138,20,20,22,20,0)	82.2 (± 145.44)	35.5 (± 78.13)	24.0 (± 33.59)	79.9 (± 118.94)
Cycle 1 Day 1:6-10 hour(n=116,111,18,16,19,16,1)	231.7 (± 109.67)	190.8 (± 96.25)	154.3 (± 69.56)	224.1 (± 109.95)
Cycle 1 Day 15:Predose(n=103,125,16,13,16,14,1)	66.6 (± 36.56)	67.2 (± 80.70)	52.1 (± 61.70)	62.9 (± 87.36)
Cycle 1 Day 15:0.5-4 hour(n=103,117,18,13,17,15,1)	129.3 (± 109.72)	122.4 (± 114.62)	93.1 (± 117.35)	275.3 (± 305.30)
Cycle 1 Day 15:6-10 hour(n=99,104,17,13,15,15,1)	271.3 (± 103.60)	206.3 (± 97.29)	241.8 (± 241.52)	266.8 (± 146.41)
Cycle 2 Day 1:Predose(n=109,134,20,17,19,13,1)	57.2 (± 60.58)	54.6 (± 64.43)	49.2 (± 46.63)	51.6 (± 66.72)
Cycle 2 Day 1:2-12 hour(n=101,120,17,13,15,9,0)	199.7 (± 155.08)	171.7 (± 119.34)	218.6 (± 83.83)	295.0 (± 190.80)
Cycle 3 Day 1:Predose(n=105,128,17,15,18,12,0)	53.2 (± 59.53)	59.0 (± 67.58)	62.8 (± 65.77)	99.4 (± 132.33)
Cycle 4 Day 1:Predose(n=100,124,15,15,18,11,1)	50.7 (± 52.16)	56.0 (± 61.56)	65.8 (± 115.31)	53.4 (± 81.66)

Cycle 5 Day 1:Predose(n=88,121,14,12,17,11,0)	53.5 (± 56.69)	52.1 (± 65.15)	60.8 (± 58.38)	71.8 (± 134.39)
Cycle 6 Day 1:Predose(n=79,111,13,10,14,8,0)	40.6 (± 33.66)	51.8 (± 49.19)	114.0 (± 189.97)	49.9 (± 68.97)

End point values	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	1	
Units: mcg/L				
arithmetic mean (standard deviation)				
Cycle 1 Day 1:0.5-4 hour(n=122,138,20,20,22,20,0)	41.8 (± 100.34)	123.8 (± 169.05)	99999 (± 99999)	
Cycle 1 Day 1:6-10 hour(n=116,111,18,16,19,16,1)	169.7 (± 95.78)	214.2 (± 86.51)	116 (± 99999)	
Cycle 1 Day 15:Predose(n=103,125,16,13,16,14,1)	60.9 (± 46.38)	61.1 (± 69.54)	52.2 (± 99999)	
Cycle 1 Day 15:0.5-4 hour(n=103,117,18,13,17,15,1)	142.8 (± 149.90)	153.9 (± 135.79)	45.9 (± 99999)	
Cycle 1 Day 15:6-10 hour(n=99,104,17,13,15,15,1)	210.6 (± 78.37)	249.7 (± 91.65)	161 (± 99999)	
Cycle 2 Day 1:Predose(n=109,134,20,17,19,13,1)	42.0 (± 48.16)	22.3 (± 21.61)	26.1 (± 99999)	
Cycle 2 Day 1:2-12 hour(n=101,120,17,13,15,9,0)	166.5 (± 128.95)	204.7 (± 174.60)	99999 (± 99999)	
Cycle 3 Day 1:Predose(n=105,128,17,15,18,12,0)	43.7 (± 50.45)	37.9 (± 29.19)	99999 (± 99999)	
Cycle 4 Day 1:Predose(n=100,124,15,15,18,11,1)	34.3 (± 54.94)	18.8 (± 34.33)	61.9 (± 99999)	
Cycle 5 Day 1:Predose(n=88,121,14,12,17,11,0)	37.7 (± 42.97)	39.0 (± 29.50)	99999 (± 99999)	
Cycle 6 Day 1:Predose(n=79,111,13,10,14,8,0)	36.9 (± 34.12)	34.2 (± 31.86)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose of the study drug up to 30 days after the last dose (up to 74 months)

Adverse event reporting additional description:

The safety analysis set included all subjects who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC

Reporting group description:

Subjects with RCC received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC

Reporting group description:

Subjects with EC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC

Reporting group description:

Subjects with RCC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma

Reporting group description:

Subjects with Leiomyosarcoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC

Reporting group description:

Subjects with NSCLC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC

Reporting group description:

Subject with HNSCC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC

Reporting group description:

Subjects with UC received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC

Reporting group description:

Subject with NSCLC received lenvatinib 24 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Reporting group title	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma

Reporting group description:

Subjects with Melanoma received lenvatinib 20 mg/day, capsules, orally, once daily in combination with pembrolizumab 200 mg, intravenous, infusion, Q3W on Day 1 of each cycle (cycle length=21 days) until PD, development of unacceptable toxicity, subject choice, withdrawal of consent, lost to follow up or discontinuation of this study by the sponsor.

Serious adverse events	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	73 / 124 (58.87%)	81 / 145 (55.86%)
number of deaths (all causes)	1	88	74
number of deaths resulting from adverse events	0	9	13
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Malignant pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Tumour associated fever			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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			
Arteriosclerosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	4 / 145 (2.76%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	8 / 124 (6.45%)	5 / 145 (3.45%)
occurrences causally related to treatment / all	0 / 0	8 / 9	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pyrexia			

subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Female genital tract fistula			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Aspiration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	6 / 145 (4.14%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated pneumonitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Laryngeal haemorrhage			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal inflammation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	0 / 124 (0.00%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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	0 / 2 (0.00%)	1 / 124 (0.81%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 oedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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			
Mental status changes			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	3 / 124 (2.42%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Amylase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Troponin increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural oedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal compression fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hypobarism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 pseudoaneurysm			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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			
Acute coronary syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 myocardial infarction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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 failure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac arrest			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Angina pectoris			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Atrial tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 failure congestive			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Intracardiac thrombus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	1 / 124 (0.81%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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			
Encephalopathy			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	3 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Headache			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hydrocephalus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Nervous system disorder			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Ruptured cerebral aneurysm			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	4 / 145 (2.76%)
occurrences causally related to treatment / all	0 / 0	1 / 9	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Anal fistula			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Colitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 haemorrhage			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Gastrointestinal perforation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal ulcer			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Large intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Jejunal perforation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ulcer perforation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pneumoperitoneum			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Pancreatitis			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	3 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 ulcer haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Small intestinal obstruction			

subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Small intestinal perforation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hepatic failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune-mediated hepatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Portal vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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			
Drug eruption			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 ulcer			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Rash maculo-papular			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	6 / 145 (4.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	5 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			

subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Renal failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 impairment			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Urinary retention			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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			
Adrenal insufficiency			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	3 / 3	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myopathy toxic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridial sepsis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (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
Abscess limb			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
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 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Abscess oral			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Epiglottitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Groin infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Necrotising fasciitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	6 / 145 (4.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Peritonitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Pelvic abscess			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Psoas abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
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 / 2 (0.00%)	3 / 124 (2.42%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	6 / 145 (4.14%)
occurrences causally related to treatment / all	0 / 0	1 / 2	5 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hypomagnesaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (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
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	2 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	15 / 21 (71.43%)	12 / 22 (54.55%)
number of deaths (all causes)	1	16	15
number of deaths resulting from adverse events	0	4	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 associated fever			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			
Arteriosclerosis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atelectasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated pneumonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Pneumonitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Pneumothorax spontaneous			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
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 oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			
Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			

Post procedural oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypobarism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 pseudoaneurysm			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
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 disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Acute myocardial infarction			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 congestive			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			
Encephalopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			

subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Dysarthria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 tonic-clonic seizure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Hypertensive encephalopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			

subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Nervous system disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ruptured cerebral aneurysm			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jejunal perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 ulcer perforation			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Proctalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 ulcer haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			
Cholecystitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Hepatic failure			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Erythema			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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			

Acute kidney injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 impairment			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
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			
Adrenal insufficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myopathy toxic			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Flank pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridial sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
COVID-19 pneumonia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess oral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Anorectal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin infection			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
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 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)	1 / 1 (100.00%)	12 / 21 (57.14%)
number of deaths (all causes)	16	1	15
number of deaths resulting from	5	0	2

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Cancer pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 associated fever			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Arteriosclerosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Asthenia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Female genital tract fistula			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypoxia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated pneumonitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal inflammation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pneumonitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Pneumothorax			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 spontaneous			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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 oedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Confusional state			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Blood bilirubin increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 creatinine increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Post procedural oedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypobarism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
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 pseudoaneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			

Acute coronary syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 myocardial infarction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 congestive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Coronary artery disease			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Encephalopathy			
subjects affected / exposed	0 / 20 (0.00%)	1 / 1 (100.00%)	0 / 21 (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 ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 tonic-clonic seizure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Intraventricular haemorrhage			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 sensory neuropathy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ruptured cerebral aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Thrombocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain upper			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 fistula			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Gastrointestinal perforation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jejunal perforation			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 ulcer perforation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Small intestinal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 ulcer haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Drug eruption			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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			
Acute kidney injury			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (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
Haematuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Proteinuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 impairment			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myopathy toxic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pathological fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridial sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess oral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal haemorrhagic			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 abscess			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 abscess			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Psoas abscess			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Post procedural infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (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
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Wound infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
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 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: RCC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: EC	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: RCC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	122 / 124 (98.39%)	145 / 145 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 2 (100.00%)	75 / 124 (60.48%)	66 / 145 (45.52%)
occurrences (all)	2	173	175
Flushing			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences (all)	0	3	1
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	10 / 124 (8.06%)	12 / 145 (8.28%)
occurrences (all)	0	13	13
Peripheral embolism			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	2 / 145 (1.38%)
occurrences (all)	0	1	2
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	1 / 145 (0.69%)
occurrences (all)	0	3	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 2 (100.00%)	66 / 124 (53.23%)	95 / 145 (65.52%)
occurrences (all)	6	159	261
Gait disturbance			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	0 / 145 (0.00%)
occurrences (all)	0	6	0
Cyst			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 2 (0.00%)	14 / 124 (11.29%)	11 / 145 (7.59%)
occurrences (all)	0	16	12

Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	22 / 124 (17.74%)	6 / 145 (4.14%)
occurrences (all)	0	70	12
Non-cardiac chest pain			
subjects affected / exposed	0 / 2 (0.00%)	8 / 124 (6.45%)	5 / 145 (3.45%)
occurrences (all)	0	8	5
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	29 / 124 (23.39%)	27 / 145 (18.62%)
occurrences (all)	0	38	37
Pain			
subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	15 / 145 (10.34%)
occurrences (all)	0	6	18
Temperature intolerance			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	10 / 145 (6.90%)
occurrences (all)	0	1	12
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	13 / 124 (10.48%)	21 / 145 (14.48%)
occurrences (all)	0	16	28
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	0 / 2 (0.00%)	10 / 124 (8.06%)	0 / 145 (0.00%)
occurrences (all)	0	10	0
Pelvic pain			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	0 / 145 (0.00%)
occurrences (all)	0	6	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	2 / 2 (100.00%)	37 / 124 (29.84%)	59 / 145 (40.69%)
occurrences (all)	4	62	78
Hiccups			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	1 / 2 (50.00%)	9 / 124 (7.26%)	28 / 145 (19.31%)
occurrences (all)	1	10	41
Dyspnoea exertional			

subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	2 / 145 (1.38%)
occurrences (all)	0	3	2
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	22 / 124 (17.74%)	43 / 145 (29.66%)
occurrences (all)	0	26	68
Cough			
subjects affected / exposed	0 / 2 (0.00%)	33 / 124 (26.61%)	67 / 145 (46.21%)
occurrences (all)	0	44	103
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	13 / 124 (10.48%)	21 / 145 (14.48%)
occurrences (all)	0	21	32
Haemoptysis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences (all)	0	0	2
Hypoxia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	9 / 124 (7.26%)	24 / 145 (16.55%)
occurrences (all)	0	12	31
Upper-airway cough syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	10 / 145 (6.90%)
occurrences (all)	0	0	11
Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	27 / 145 (18.62%)
occurrences (all)	0	0	47
Rhinitis allergic			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	8 / 145 (5.52%)
occurrences (all)	0	1	8
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	3 / 145 (2.07%)
occurrences (all)	0	0	3
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	7 / 145 (4.83%)
occurrences (all)	0	2	8
Sneezing			

subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	13 / 145 (8.97%)
occurrences (all)	0	0	15
Wheezing			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	4 / 145 (2.76%)
occurrences (all)	0	3	5
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	2 / 145 (1.38%)
occurrences (all)	0	6	2
Depression			
subjects affected / exposed	0 / 2 (0.00%)	9 / 124 (7.26%)	5 / 145 (3.45%)
occurrences (all)	0	10	5
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	14 / 124 (11.29%)	24 / 145 (16.55%)
occurrences (all)	0	18	29
Mental status changes			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	0 / 145 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	9 / 124 (7.26%)	11 / 145 (7.59%)
occurrences (all)	0	10	11
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	15 / 124 (12.10%)	18 / 145 (12.41%)
occurrences (all)	3	28	33
Liver function test increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	1 / 2 (50.00%)	45 / 124 (36.29%)	46 / 145 (31.72%)
occurrences (all)	1	103	79
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	17 / 124 (13.71%)	18 / 145 (12.41%)
occurrences (all)	0	37	35
Amylase increased			

subjects affected / exposed	0 / 2 (0.00%)	7 / 124 (5.65%)	20 / 145 (13.79%)
occurrences (all)	0	20	67
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	14 / 124 (11.29%)	17 / 145 (11.72%)
occurrences (all)	0	21	31
Blood bilirubin increased			
subjects affected / exposed	0 / 2 (0.00%)	9 / 124 (7.26%)	7 / 145 (4.83%)
occurrences (all)	0	12	7
Platelet count decreased			
subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	7 / 145 (4.83%)
occurrences (all)	0	7	9
Blood cholesterol increased			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	9 / 145 (6.21%)
occurrences (all)	0	8	14
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	13 / 124 (10.48%)	29 / 145 (20.00%)
occurrences (all)	0	26	71
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	8 / 145 (5.52%)
occurrences (all)	0	0	8
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	12 / 145 (8.28%)
occurrences (all)	0	3	15
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 2 (0.00%)	8 / 124 (6.45%)	6 / 145 (4.14%)
occurrences (all)	0	9	11
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	20 / 124 (16.13%)	32 / 145 (22.07%)
occurrences (all)	0	44	114
Lymphocyte count decreased			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	4 / 145 (2.76%)
occurrences (all)	0	4	11
Neutrophil count decreased			

subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	1 / 145 (0.69%)
occurrences (all)	0	2	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	13 / 145 (8.97%)
occurrences (all)	0	2	16
Fall			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	8 / 145 (5.52%)
occurrences (all)	0	7	12
Stoma site haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	1	0	0
Ventricular arrhythmia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	1	0	0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences (all)	0	1	1
Palpitations			
subjects affected / exposed	0 / 2 (0.00%)	7 / 124 (5.65%)	4 / 145 (2.76%)
occurrences (all)	0	10	4
Cardiac failure congestive			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences (all)	0	1	1
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 2 (0.00%)	42 / 124 (33.87%)	44 / 145 (30.34%)
occurrences (all)	0	62	65
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	19 / 124 (15.32%)	30 / 145 (20.69%)
occurrences (all)	0	24	38
Dysgeusia			
subjects affected / exposed	0 / 2 (0.00%)	14 / 124 (11.29%)	20 / 145 (13.79%)
occurrences (all)	0	19	24
Dizziness postural			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	2 / 145 (1.38%)
occurrences (all)	0	0	2
Tremor			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	3 / 145 (2.07%)
occurrences (all)	0	6	3
Somnolence			
subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	1 / 145 (0.69%)
occurrences (all)	0	5	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 2 (0.00%)	11 / 124 (8.87%)	10 / 145 (6.90%)
occurrences (all)	0	12	11
Metabolic encephalopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	11 / 124 (8.87%)	19 / 145 (13.10%)
occurrences (all)	0	16	31
Thrombocytopenia			
subjects affected / exposed	0 / 2 (0.00%)	9 / 124 (7.26%)	0 / 145 (0.00%)
occurrences (all)	0	17	0
Eye disorders			

Vision blurred			
subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	8 / 145 (5.52%)
occurrences (all)	0	6	8
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 2 (50.00%)	41 / 124 (33.06%)	43 / 145 (29.66%)
occurrences (all)	1	50	55
Diarrhoea			
subjects affected / exposed	2 / 2 (100.00%)	79 / 124 (63.71%)	97 / 145 (66.90%)
occurrences (all)	4	270	330
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	12 / 124 (9.68%)	21 / 145 (14.48%)
occurrences (all)	0	13	30
Abdominal distension			
subjects affected / exposed	1 / 2 (50.00%)	10 / 124 (8.06%)	7 / 145 (4.83%)
occurrences (all)	2	13	8
Nausea			
subjects affected / exposed	2 / 2 (100.00%)	66 / 124 (53.23%)	74 / 145 (51.03%)
occurrences (all)	2	144	132
Stomatitis			
subjects affected / exposed	2 / 2 (100.00%)	45 / 124 (36.29%)	63 / 145 (43.45%)
occurrences (all)	4	79	109
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	56 / 124 (45.16%)	44 / 145 (30.34%)
occurrences (all)	2	137	84
Abdominal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	8 / 145 (5.52%)
occurrences (all)	0	3	11
Gingival bleeding			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	8 / 145 (5.52%)
occurrences (all)	0	2	9
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	18 / 124 (14.52%)	9 / 145 (6.21%)
occurrences (all)	0	21	9
Flatulence			

subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	15 / 145 (10.34%)
occurrences (all)	0	5	16
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)	11 / 124 (8.87%)	5 / 145 (3.45%)
occurrences (all)	0	15	6
Dry mouth			
subjects affected / exposed	0 / 2 (0.00%)	22 / 124 (17.74%)	20 / 145 (13.79%)
occurrences (all)	0	30	23
Colitis			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	5 / 145 (3.45%)
occurrences (all)	0	6	5
Anorectal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	1 / 145 (0.69%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	12 / 124 (9.68%)	14 / 145 (9.66%)
occurrences (all)	0	16	24
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	38 / 124 (30.65%)	37 / 145 (25.52%)
occurrences (all)	0	58	52
Gingival pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	5 / 145 (3.45%)
occurrences (all)	0	2	7
Haemorrhoids			
subjects affected / exposed	0 / 2 (0.00%)	9 / 124 (7.26%)	3 / 145 (2.07%)
occurrences (all)	0	9	3
Toothache			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	13 / 145 (8.97%)
occurrences (all)	0	6	17
Proctalgia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	3 / 145 (2.07%)
occurrences (all)	0	3	3
Oral pain			
subjects affected / exposed	0 / 2 (0.00%)	11 / 124 (8.87%)	11 / 145 (7.59%)
occurrences (all)	0	15	12
Oesophagitis			

subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	2 / 145 (1.38%)
occurrences (all)	0	2	2
Cheilitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 2 (50.00%)	4 / 124 (3.23%)	2 / 145 (1.38%)
occurrences (all)	2	5	3
Night sweats			
subjects affected / exposed	1 / 2 (50.00%)	1 / 124 (0.81%)	8 / 145 (5.52%)
occurrences (all)	1	1	13
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	8 / 145 (5.52%)
occurrences (all)	0	6	8
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 2 (0.00%)	34 / 124 (27.42%)	46 / 145 (31.72%)
occurrences (all)	0	80	112
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	19 / 124 (15.32%)	21 / 145 (14.48%)
occurrences (all)	0	22	28
Rash			
subjects affected / exposed	0 / 2 (0.00%)	10 / 124 (8.06%)	25 / 145 (17.24%)
occurrences (all)	0	22	37
Rash erythematous			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	4 / 145 (2.76%)
occurrences (all)	0	0	5
Rash maculo-papular			
subjects affected / exposed	0 / 2 (0.00%)	20 / 124 (16.13%)	25 / 145 (17.24%)
occurrences (all)	0	36	44
Alopecia			
subjects affected / exposed	0 / 2 (0.00%)	11 / 124 (8.87%)	4 / 145 (2.76%)
occurrences (all)	0	12	5
Dermatitis acneiform			

subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	11 / 145 (7.59%)
occurrences (all)	0	4	12
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)	15 / 124 (12.10%)	26 / 145 (17.93%)
occurrences (all)	0	16	33
Rash pruritic			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	2 / 145 (1.38%)
occurrences (all)	0	1	2
Skin exfoliation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	2 / 145 (1.38%)
occurrences (all)	0	1	2
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 2 (50.00%)	37 / 124 (29.84%)	67 / 145 (46.21%)
occurrences (all)	1	121	168
Dysuria			
subjects affected / exposed	0 / 2 (0.00%)	7 / 124 (5.65%)	4 / 145 (2.76%)
occurrences (all)	0	8	5
Pollakiuria			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	11 / 145 (7.59%)
occurrences (all)	0	7	11
Nocturia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	9 / 145 (6.21%)
occurrences (all)	0	0	9
Hydronephrosis			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	1 / 145 (0.69%)
occurrences (all)	0	3	1
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	12 / 145 (8.28%)
occurrences (all)	0	8	16
Urinary retention			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	3 / 145 (2.07%)
occurrences (all)	0	0	3

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 2 (50.00%)	61 / 124 (49.19%)	60 / 145 (41.38%)
occurrences (all)	1	77	66
Hyperthyroidism			
subjects affected / exposed	0 / 2 (0.00%)	7 / 124 (5.65%)	6 / 145 (4.14%)
occurrences (all)	0	7	7
Adrenal insufficiency			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	10 / 145 (6.90%)
occurrences (all)	0	2	10
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 2 (50.00%)	25 / 124 (20.16%)	36 / 145 (24.83%)
occurrences (all)	2	38	47
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	49 / 124 (39.52%)	70 / 145 (48.28%)
occurrences (all)	0	99	123
Myalgia			
subjects affected / exposed	1 / 2 (50.00%)	28 / 124 (22.58%)	20 / 145 (13.79%)
occurrences (all)	1	39	39
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	15 / 124 (12.10%)	28 / 145 (19.31%)
occurrences (all)	0	20	49
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	8 / 145 (5.52%)
occurrences (all)	0	8	8
Musculoskeletal pain			
subjects affected / exposed	0 / 2 (0.00%)	20 / 124 (16.13%)	20 / 145 (13.79%)
occurrences (all)	0	26	31
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	8 / 145 (5.52%)
occurrences (all)	0	4	12
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	13 / 124 (10.48%)	13 / 145 (8.97%)
occurrences (all)	0	14	15
Muscle spasms			

subjects affected / exposed	0 / 2 (0.00%)	13 / 124 (10.48%)	17 / 145 (11.72%)
occurrences (all)	0	18	24
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	10 / 145 (6.90%)
occurrences (all)	0	5	17
Bone pain			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	3 / 145 (2.07%)
occurrences (all)	0	2	4
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	1	0	0
Osteomyelitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	2 / 2 (100.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	4	0	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	37 / 124 (29.84%)	8 / 145 (5.52%)
occurrences (all)	0	59	19
Oral candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	2 / 145 (1.38%)
occurrences (all)	0	7	2
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	8 / 145 (5.52%)
occurrences (all)	0	1	8
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	2 / 145 (1.38%)
occurrences (all)	0	2	2
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	1 / 145 (0.69%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	5 / 124 (4.03%)	2 / 145 (1.38%)
occurrences (all)	0	5	2

Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	8 / 124 (6.45%)	4 / 145 (2.76%)
occurrences (all)	0	12	4
Soft tissue infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 2 (0.00%)	4 / 124 (3.23%)	4 / 145 (2.76%)
occurrences (all)	0	5	6
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	14 / 124 (11.29%)	9 / 145 (6.21%)
occurrences (all)	0	17	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 2 (100.00%)	68 / 124 (54.84%)	70 / 145 (48.28%)
occurrences (all)	3	135	114
Hyponatraemia			
subjects affected / exposed	1 / 2 (50.00%)	15 / 124 (12.10%)	21 / 145 (14.48%)
occurrences (all)	1	21	47
Hypomagnesaemia			
subjects affected / exposed	1 / 2 (50.00%)	35 / 124 (28.23%)	20 / 145 (13.79%)
occurrences (all)	1	65	44
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	19 / 124 (15.32%)	10 / 145 (6.90%)
occurrences (all)	0	33	12
Hypocalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	4 / 145 (2.76%)
occurrences (all)	0	3	4
Hypoalbuminaemia			
subjects affected / exposed	0 / 2 (0.00%)	8 / 124 (6.45%)	2 / 145 (1.38%)
occurrences (all)	0	8	5
Hypertriglyceridaemia			
subjects affected / exposed	0 / 2 (0.00%)	6 / 124 (4.84%)	29 / 145 (20.00%)
occurrences (all)	0	11	102
Dehydration			

subjects affected / exposed	0 / 2 (0.00%)	17 / 124 (13.71%)	11 / 145 (7.59%)
occurrences (all)	0	23	17
Hyperglycaemia			
subjects affected / exposed	0 / 2 (0.00%)	8 / 124 (6.45%)	11 / 145 (7.59%)
occurrences (all)	0	10	12
Hypercalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 124 (1.61%)	11 / 145 (7.59%)
occurrences (all)	0	2	13
Electrolyte imbalance			
subjects affected / exposed	0 / 2 (0.00%)	0 / 124 (0.00%)	0 / 145 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 2 (0.00%)	3 / 124 (2.42%)	12 / 145 (8.28%)
occurrences (all)	0	3	16
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 124 (0.81%)	15 / 145 (10.34%)
occurrences (all)	0	1	32

Non-serious adverse events	Phase1b/2,Lenvatinib20mg/day+Pembrolizumab200mg:Leiomyosarcoma	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg:NSCLC	Phase 1b/ 2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:HNSCC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	21 / 21 (100.00%)	22 / 22 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 1 (100.00%)	8 / 21 (38.10%)	8 / 22 (36.36%)
occurrences (all)	2	25	16
Flushing			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	3 / 22 (13.64%)
occurrences (all)	0	1	3
Peripheral embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			

subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 1 (100.00%)	15 / 21 (71.43%)	11 / 22 (50.00%)
occurrences (all)	1	33	25
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Cyst			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	3 / 22 (13.64%)
occurrences (all)	0	12	4
Pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Temperature intolerance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			

Vaginal discharge			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	6 / 22 (27.27%)
occurrences (all)	0	9	6
Hiccups			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	8 / 21 (38.10%)	4 / 22 (18.18%)
occurrences (all)	0	17	6
Cough			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	7 / 22 (31.82%)
occurrences (all)	0	8	8
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	1 / 22 (4.55%)
occurrences (all)	0	4	3
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	4 / 22 (18.18%)
occurrences (all)	0	1	5
Hypoxia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Oropharyngeal pain			

subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	7 / 22 (31.82%)
occurrences (all)	0	3	21
Upper-airway cough syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Productive cough			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	4 / 21 (19.05%)	1 / 22 (4.55%)
occurrences (all)	0	5	1
Sneezing			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	0 / 22 (0.00%)
occurrences (all)	0	4	0
Depression			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	1 / 22 (4.55%)
occurrences (all)	0	5	1
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	2 / 22 (9.09%)
occurrences (all)	0	3	2
Mental status changes			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	2

Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	2 / 22 (9.09%)
occurrences (all)	0	6	2
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	4	5
Liver function test increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	7 / 21 (33.33%)	5 / 22 (22.73%)
occurrences (all)	0	21	6
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	4	1
Amylase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	3	3
Blood cholesterol increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	3
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	2	6
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Stoma site haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ventricular arrhythmia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Arteriosclerosis coronary artery			

subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Cardiac failure congestive			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	6 / 22 (27.27%)
occurrences (all)	0	3	8
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	6 / 21 (28.57%)	4 / 22 (18.18%)
occurrences (all)	0	6	4
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dizziness postural			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Lethargy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	0 / 22 (0.00%)
occurrences (all)	0	5	0
Somnolence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Peripheral sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	0	3
Metabolic encephalopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	4 / 22 (18.18%)
occurrences (all)	0	3	5
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	1 / 22 (4.55%)
occurrences (all)	0	4	1
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	7 / 21 (33.33%)	5 / 22 (22.73%)
occurrences (all)	0	9	5
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	12 / 21 (57.14%)	8 / 22 (36.36%)
occurrences (all)	0	39	26
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	10 / 21 (47.62%)	9 / 22 (40.91%)
occurrences (all)	0	18	11
Stomatitis			
subjects affected / exposed	1 / 1 (100.00%)	5 / 21 (23.81%)	7 / 22 (31.82%)
occurrences (all)	1	6	13
Vomiting			

subjects affected / exposed	1 / 1 (100.00%)	8 / 21 (38.10%)	6 / 22 (27.27%)
occurrences (all)	1	14	7
Abdominal discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	3 / 22 (13.64%)
occurrences (all)	0	2	5
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	1 / 22 (4.55%)
occurrences (all)	0	4	1
Colitis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	4	1
Anorectal discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	1 / 22 (4.55%)
occurrences (all)	0	6	2
Gingival pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	3
Haemorrhoids			

subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Proctalgia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Oral pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	6 / 22 (27.27%)
occurrences (all)	0	1	22
Oesophagitis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	3	1
Cheilitis			
subjects affected / exposed	1 / 1 (100.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Night sweats			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	4 / 22 (18.18%)
occurrences (all)	0	0	7
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	6 / 21 (28.57%)	2 / 22 (9.09%)
occurrences (all)	0	13	2
Rash			

subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	2 / 22 (9.09%)
occurrences (all)	0	6	2
Rash erythematous			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	3 / 22 (13.64%)
occurrences (all)	0	1	3
Rash pruritic			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Skin exfoliation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Skin lesion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)	8 / 21 (38.10%)	5 / 22 (22.73%)
occurrences (all)	0	23	20
Dysuria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	1	4
Pollakiuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	4

Nocturia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 1 (0.00%)	8 / 21 (38.10%)	6 / 22 (27.27%)
occurrences (all)	0	8	7
Hyperthyroidism			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	2
Adrenal insufficiency			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	2 / 22 (9.09%)
occurrences (all)	0	6	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	4 / 21 (19.05%)	3 / 22 (13.64%)
occurrences (all)	0	6	3
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	8 / 21 (38.10%)	4 / 22 (18.18%)
occurrences (all)	0	16	4
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	4 / 21 (19.05%)	1 / 22 (4.55%)
occurrences (all)	0	6	1
Neck pain			

subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	1	2
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	1 / 22 (4.55%)
occurrences (all)	0	4	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	1	3
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	1 / 22 (4.55%)
occurrences (all)	0	6	1
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	3	3
Flank pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Osteomyelitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	3 / 21 (14.29%)	2 / 22 (9.09%)
occurrences (all)	0	5	4
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	3 / 22 (13.64%)
occurrences (all)	0	1	3

Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 21 (9.52%)	1 / 22 (4.55%)
occurrences (all)	0	3	2
Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	4 / 21 (19.05%)	2 / 22 (9.09%)
occurrences (all)	0	4	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	16 / 21 (76.19%)	10 / 22 (45.45%)
occurrences (all)	0	30	14
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	4 / 22 (18.18%)
occurrences (all)	0	9	10
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 21 (19.05%)	2 / 22 (9.09%)
occurrences (all)	0	4	2
Hypokalaemia			

subjects affected / exposed	0 / 1 (0.00%)	5 / 21 (23.81%)	1 / 22 (4.55%)
occurrences (all)	0	8	1
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	0	1	4
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	4 / 21 (19.05%)	1 / 22 (4.55%)
occurrences (all)	0	8	1
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1b/2, Lenvatinib 20 mg/day+Pembrolizumab 200 mg: UC	Phase 1b, Lenvatinib 24 mg/day + Pembrolizumab 200 mg: NSCLC	Phase 1b/2,Lenvatinib 20 mg/day+Pembrolizumab 200 mg:Melanoma
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	1 / 1 (100.00%)	21 / 21 (100.00%)
Vascular disorders			

Hypertension			
subjects affected / exposed	9 / 20 (45.00%)	1 / 1 (100.00%)	9 / 21 (42.86%)
occurrences (all)	15	2	12
Flushing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Peripheral embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 20 (60.00%)	1 / 1 (100.00%)	14 / 21 (66.67%)
occurrences (all)	21	3	21
Gait disturbance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Cyst			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	2	0	2
Asthenia			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	6	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	6 / 20 (30.00%)	0 / 1 (0.00%)	5 / 21 (23.81%)
occurrences (all)	16	0	6
Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Temperature intolerance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	4	0	1
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 1 (100.00%)	10 / 21 (47.62%)
occurrences (all)	3	1	12
Hiccups			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	8 / 20 (40.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	11	0	3
Cough			

subjects affected / exposed	6 / 20 (30.00%)	0 / 1 (0.00%)	4 / 21 (19.05%)
occurrences (all)	13	0	5
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Haemoptysis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	7 / 21 (33.33%)
occurrences (all)	2	0	7
Upper-airway cough syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	40	0	0
Sneezing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			

Confusional state			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	2
Insomnia			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	4 / 21 (19.05%)
occurrences (all)	7	0	4
Mental status changes			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Anxiety			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	5	0	5
Liver function test increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	6 / 20 (30.00%)	0 / 1 (0.00%)	5 / 21 (23.81%)
occurrences (all)	9	0	13
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	1	0	5
Amylase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	4
Blood bilirubin increased			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	2
Platelet count decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	2	0	1
Lipase increased			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	18	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Fall			

subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Stoma site haemorrhage			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Ventricular arrhythmia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Arteriosclerosis coronary artery			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Atrial fibrillation			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	2
Palpitations			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Cardiac failure congestive			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Bradycardia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 20 (20.00%)	1 / 1 (100.00%)	5 / 21 (23.81%)
occurrences (all)	4	2	6
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	1 / 1 (100.00%)	3 / 21 (14.29%)
occurrences (all)	2	1	4
Dysgeusia			

subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Dizziness postural			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Tremor			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Metabolic encephalopathy			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 20 (30.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	7	0	4
Thrombocytopenia			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	4	0	3
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 20 (25.00%)	0 / 1 (0.00%)	9 / 21 (42.86%)
occurrences (all)	7	0	14
Diarrhoea			

subjects affected / exposed	11 / 20 (55.00%)	1 / 1 (100.00%)	13 / 21 (61.90%)
occurrences (all)	36	3	23
Dyspepsia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 1 (100.00%)	3 / 21 (14.29%)
occurrences (all)	3	1	3
Abdominal distension			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	2
Nausea			
subjects affected / exposed	12 / 20 (60.00%)	0 / 1 (0.00%)	13 / 21 (61.90%)
occurrences (all)	19	0	24
Stomatitis			
subjects affected / exposed	2 / 20 (10.00%)	1 / 1 (100.00%)	1 / 21 (4.76%)
occurrences (all)	2	1	1
Vomiting			
subjects affected / exposed	10 / 20 (50.00%)	0 / 1 (0.00%)	9 / 21 (42.86%)
occurrences (all)	12	0	13
Abdominal discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	2	0	1
Flatulence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Dysphagia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	3	0	3
Colitis			

subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Anorectal discomfort			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Abdominal pain			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	5 / 21 (23.81%)
occurrences (all)	4	0	5
Gingival pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	2
Toothache			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Oral pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	5 / 21 (23.81%)
occurrences (all)	1	0	6
Oesophagitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Night sweats			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	0	0	3
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	4 / 21 (19.05%)
occurrences (all)	2	0	5
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	4	0	1
Rash			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	12	0	3
Rash erythematous			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	5 / 21 (23.81%)
occurrences (all)	0	0	6
Alopecia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	0	0	3
Dermatitis acneiform			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Dry skin			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Skin exfoliation			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	3
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	13 / 20 (65.00%)	1 / 1 (100.00%)	7 / 21 (33.33%)
occurrences (all)	38	2	13
Dysuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Nocturia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Haematuria			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Urinary retention			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	8 / 20 (40.00%)	1 / 1 (100.00%)	7 / 21 (33.33%)
occurrences (all)	8	1	10
Hyperthyroidism			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Adrenal insufficiency			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 20 (25.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	5	0	4
Arthralgia			
subjects affected / exposed	7 / 20 (35.00%)	1 / 1 (100.00%)	7 / 21 (33.33%)
occurrences (all)	8	2	9
Myalgia			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	3	0	3
Pain in extremity			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	4 / 21 (19.05%)
occurrences (all)	5	0	4
Neck pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	2
Musculoskeletal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	3
Musculoskeletal chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	4 / 21 (19.05%)
occurrences (all)	4	0	4
Muscle spasms			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	3	0	2
Flank pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	6	0	1
Bone pain			

subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Osteomyelitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	9 / 20 (45.00%)	1 / 1 (100.00%)	6 / 21 (28.57%)
occurrences (all)	14	1	8
Oral candidiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Bronchitis			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Soft tissue infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2

Tooth infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	6 / 21 (28.57%)
occurrences (all)	4	0	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 20 (50.00%)	1 / 1 (100.00%)	10 / 21 (47.62%)
occurrences (all)	18	1	15
Hyponatraemia			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	6	0	2
Hypomagnesaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	6	0	1
Hypokalaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	5 / 21 (23.81%)
occurrences (all)	3	0	5
Hypocalcaemia			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	7	0	1
Hypoalbuminaemia			
subjects affected / exposed	7 / 20 (35.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	13	0	0
Hypertriglyceridaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	7	0	1
Dehydration			
subjects affected / exposed	10 / 20 (50.00%)	0 / 1 (0.00%)	3 / 21 (14.29%)
occurrences (all)	12	0	3
Hyperglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Hypercalcaemia			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Electrolyte imbalance			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	2
Hypophosphataemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	4 / 21 (19.05%)
occurrences (all)	2	0	5
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 January 2016	Protocol amendment 01: Supporting language was added to align with the planned biomarker analysis in the exploratory objective. Changed dose modification guidelines for pembrolizumab-related AEs to reflect updated guidelines. Updated pembrolizumab indications and clinical results to reflect most recent information. Updated the dose modification guideline for pembrolizumab-related. AEs to the latest pembrolizumab protocol template. Specified that no formal interim analysis was used to determine if a cohort was to be expanded from 10 to 20 subjects; this decision was made based on the results of a discussion of efficacy and safety data between the investigators and the sponsor. Inclusion criterion 1 added an exception that subject who has not received nivolumab or pembrolizumab could be enrolled in this study even if nivolumab or pembrolizumab is an approved therapy.
30 March 2016	Protocol amendment 02: Limited eligibility of subjects with RCC to "predominantly clear cell" RCC only. Added general guidelines for holding periods of lenvatinib due to minor and major procedures. Revised list of approved indications for pembrolizumab based on labeling updates.
26 October 2016	Protocol amendment 03: Clarified the RP2D dose of the combination to be used in Phase 2. Exclusion criterion 20 changed to ensure exclusion of subjects with a history of noninfectious pneumonitis requiring steroid treatment and exclusion of subjects with current pneumonitis based on safety information from ongoing pembrolizumab combination clinical Studies. Separated and clarified dose modification instructions for lenvatinib-related and pembrolizumab-related toxicity. Added blood sample collection from Phase 2 subjects for potential pharmacodynamics and PG analysis. Modified efficacy and safety analysis plans to include possible analyses of the combination of lenvatinib plus pembrolizumab comparing treatment-naïve subjects versus subjects with prior lines of systemic therapy.

23 May 2017	Protocol amendment 04: Revised the definition of the end of study to the time of data cutoff for the final analysis or the time of last subject/last treatment, whichever occurs later for consistency across lenvatinib studies. Inclusion criterion #1 updated to indicate that subjects with histologically and/or cytologically confirmed metastatic selected solid tumor types with 0-2 prior lines of systemic therapy are eligible for enrollment in Phase 2. Inclusion criterion 11 modified to clarify that subjects with brain metastases at Baseline had to be off steroids for at least 28 days before starting study drug. Contraceptive language was modified to ensure compliance with current lenvatinib safety information. Clarified dose reduction recommendation for lenvatinib due to treatment-related toxicity. Revised text to clarify that brain scans had to be performed for all subjects, including those with HNSCC, at Screening, when clinically indicated, and to confirm CR within 1 week of response. Revised text to clarify timing of bone scans. Added requirement that pembrolizumab treatment be discontinued for subjects with recurrent Grade 2 pneumonitis. Revised text for management of proteinuria to ensure consistency in the management of proteinuria among the lenvatinib clinical studies. The management of hypertension section was clarified to indicate that, on the second and third recurrence of hypertension, lenvatinib administration should be interrupted, the dose should be reduced, and it should be restarted only when the subject was on a stable regimen of antihypertensive therapy and acceptable blood pressure values were recorded. Revised and clarified text for measurement of blood pressure. Clarified that subjects could receive up to 35 treatments (approximately 2 years) with pembrolizumab (subjects could be continued after discontinuation of pembrolizumab; subjects could continue lenvatinib as monotherapy after that time point).
22 December 2017	Protocol amendment 05: Option to increase enrollment in RCC cohort to up to 120 subjects in Phase 2 expansion based on results of 2 interim analyses, after 22 and 56 subjects have sufficient follow-up to be evaluated for response.Exploratory objective, endpoint, efficacy assessment to evaluate tumor response in subjects with RCC using IIR to obtain unbiased independent review results to support investigator assessments;regulatory authority expectations. Inclusion criterion 1:ensure consistent application of desired prestudy PD after prior anti-PD-1/PDL1 definition in this previously treated RCC subset; to decrease risk of including subjects with pseudo-progression.For previously treated RCC subjects, it was specified that PD-1 treatment progression was defined by meeting all of following criteria:a)Had received at least 2 doses of an approved anti-PD- 1/PD-L1 mAb,b)Had demonstrated PD after PD- 1/PD-L1 as RECIST 1.1.Initial evidence of PD was to be confirmed by second assessment no less than 4 weeks from date of first documented PD, in absence of rapid clinical progression,c).PD had been documented within 12 weeks from last dose of anti-PD-1/PD-L1 mAb (refractory disease) or >=12 weeks from last dose of anti-PD-1/PD-L1 mAb. All previously treated subjects must have progressed prestudy to be eligible for enrollment in Phase 2.Exclusion criterion 17, exclusion of prior treatment with any anti-PD-1 or anti-PD-L1 agent does not apply for previously treated RCC subset where prior treatment with 1 regimen containing an anti-PD-1/PD-L1 mAb was required,that there were no exceptions for prior lenvatinib treatment.Updated 200-mg pembrolizumab dose justification, treatment guidelines for Grades 3 or 4 infusion reaction, supportive care guidelines for pembrolizumab based on updated information.Added collection of Karnofsky Performance Status at Screening for RCC subjects only.Updated dataset definition, safety; efficacy subgroup analyses, sample size rationale for RCC cohort.

31 July 2018	Protocol amendment 06: Increased planned number of investigational sites to up to 25 sites in the US and EU to accommodate planned expansion of RCC cohort to approximately 120 evaluable subjects. Assessments of tumor response based on IIR using RECIST 1.1 for subjects with EC and for subjects with RCC were added to the exploratory objectives, and exploratory efficacy assessments were added to the corresponding exploratory endpoint. Modified the Phase 2 expansion of enrollment in the RCC cohort to cap the number of treatment-naïve subjects at approximately 12 and to increase the number of previously treated subjects who progressed on or after treatment with an anti-PD-1/PD-L1 agent to 33. Exclusion Criterion 12 revised to clarify that subjects who have had an allogenic tissue/solid organ transplant were to be excluded based on the updated pembrolizumab label. Clarified that 11 treatment-naïve RCC subjects included in the first interim analysis plus the 45 additional RCC subjects enrolled after completion of the first interim analysis were included in the second interim analysis and that further expansion of the RCC cohort would be limited to previously treated subjects with RCC who progressed on or after an anti-PD-1/PD-L1 treatment. Specified that available mutation status, including MMR or MSI status, was collected on the CRF. Adjusted the ORR estimate and 2-sided 95% CI of the ORR for the second analysis based on updated enrollment numbers.
19 April 2019	Protocol amendment 07: Increased RCC cohort from approximately 120 to approximately 145 evaluable subjects. Inclusion criterion #1 updated to clarify that initial RECIST 1.1 evidence of PD prestudy is to be confirmed by a second assessment in all subjects. Added information to justify that the increase in sample size of subjects with RCC improves the 95% CI of the ORR. Clarified that the regimen with an anti-PD-1/PD-L1 mAb must be the most recent therapy.
24 August 2020	Protocol amendment 08: Clarified that IIR is no longer required after final efficacy analysis data cut. Added text to allow for potential IIR of pre-Baseline scans for confirmed progression in subjects who were pretreated with anti-PD-1/PD-L1 mAb in the RCC cohort. Removed the PK/pharmacodynamic analyses as objectives of the study. Clarified that PK profile for lenvatinib in combination with pembrolizumab from this study will be compared graphically to that from subjects with different tumor types from completed studies of those receiving lenvatinib monotherapy. Scans acquired after data cutoff for final efficacy analysis, in any cohort were no longer sent to the imaging core laboratory. In addition, for enrolled subjects who were previously treated with anti PD-1/PD-L1 mAb, available pre-baseline scans were collected by sites.
30 July 2021	Protocol amendment 09: Revised and added text to clarify when treatment in study would be discontinued, subject choice, completion of 35 treatments (approximately 2 years) with pembrolizumab and lost to follow up. Subjects who discontinued pembrolizumab for any reason and were still receiving Lenvatinib study drug, will be transitioned to commercial lenvatinib if local country regulations permit. Frequency of tumor assessments in Phase Ib and Phase 2 Extension Phase per local standard of care but not less frequent than every 6 months. Tumor assessments will not be collected during Follow-Up period of Extension Phase. Follow- Up Period will consist of Off-Tx Visit. Sponsor has decided to terminate survival follow-up for all subjects currently in survival follow-up. Survival follow-up data will no longer be collected after Off- Tx Visit and after 30 days from last dose of study drugs. To clarify that subjects who undergo Off-Tx visit will undergo safety follow-up for AEs for 30 days from last dose of study treatment and for SAEs 90 days after last dose or 30 days following last dose if subject initiates new anticancer therapy, whichever is earlier. Pre-baseline scans will no longer need to be provided for RCC cohort. All study related medical or dental decisions must be made by an investigator who is qualified physician. Oral examinations to be conducted during physical examinations prior to and periodically during Lenvatinib treatment. Text for collecting and reporting death. All deaths will be collected for 30 days following last dose of study treatment and reported on Survival Case Report Form. Added text for monitoring QT prolongation and method used to calculate QTc. Clarify investigator assessment will be based upon institutional reports. Frequency of MUGA/ECHO scans in Phase Ib and Phase 2 Extension Phase to "as clinically indicated". Frequency of Weight and Body temperature in Phase 1b and Phase 2 Extension Phase to "as clinically indicated".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported