Clinical trial results:
A Phase I, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of Atezolizumab (MPDL3280A) Administered Intravenously as a Single Agent to Patients With Locally Advanced or Metastatic Solid Tumors or Hematologic Malignancies

Summary

EudraCT number	2011-001422-23
Trial protocol	GB
Global end of trial date	30 September 2018

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	PCD4989g

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01375842
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and tolerability of atezolizumab administered by intravenous (IV) infusion every 3 weeks (q3w) to patients with locally advanced or metastatic solid tumors or hematologic malignancies.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 June 2011
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	Spain: 39
Country: Number of subjects enrolled	France: 87
Country: Number of subjects enrolled	United Kingdom: 54
Country: Number of subjects enrolled	United States: 478
Worldwide total number of subjects	658
EEA total number of subjects	180

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)	394
From 65 to 84 years	261

85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 21 centers in 4 countries, comprising the US (16 centers), France (3 centers), Great Britain (1 center), and Spain (1 center).

Pre-assignment

Screening details:

A total of 955 subjects were screened for entry into the study. 295 subjects failed screening and were not enrolled into the study. 660 subjects were enrolled into the study (intent-to-treat [ITT] population). 658 subjects received any amount of atezolizumab on study (safety-evaluable population) and are reported here.

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	Dose Escalation Cohort: Atezolizumab <=1 mg/kg

Arm description:

Subjects received intravenous (IV) infusion of atezolizumab <=1 milligrams per kilogram (mg/kg) every 3 weeks (q3w) until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at <=1 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm title	Dose Escalation Cohort: Atezolizumab 3 mg/kg

Arm description:

Subjects received IV infusion of atezolizumab 3 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at 3 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm title	Dose Escalation Cohort: Atezolizumab 10 mg/kg

Arm description:

Subjects received IV infusion of atezolizumab 10 mg/kg q3w until DLT is reached or up to end of study

or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at 10 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm title	Dose Escalation Cohort: Atezolizumab 15 mg/kg

Arm description:

Subjects received IV infusion of atezolizumab 15 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at 15 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm title	Dose Escalation Cohort: Atezolizumab 20 mg/kg

Arm description:

Subjects received IV infusion of atezolizumab 20 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at 20 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm title	Expansion Cohort: Atezolizumab 1200 mg

Arm description:

Subjects received IV infusion of atezolizumab 1200 mg q3w up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered as IV infusion at 1200 mg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever

occurs first.

Number of subjects in period 1	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg
Started	9	3	36
Completed	0	0	0
Not completed	9	3	36
Physician decision	1	-	2
Consent withdrawn by subject	-	1	1
Non-Compliance	-	-	-
Study Terminated By Sponsor	1	1	6
Death	1	-	13
Progressive Disease	5	1	12
Unknown	-	-	-
Lost to follow-up	1	-	2

Number of subjects in period 1	Dose Escalation Cohort: Atezolizumab 15 mg/kg	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg
Started	236	146	228
Completed	0	0	0
Not completed	236	146	228
Physician decision	10	10	-
Consent withdrawn by subject	11	5	2
Non-Compliance	-	1	-
Study Terminated By Sponsor	34	14	24
Death	85	39	181
Progressive Disease	87	73	7
Unknown	3	-	-
Lost to follow-up	6	4	14

Baseline characteristics

Reporting groups	
Reporting group title	Dose Escalation Cohort: Atezolizumab <=1 mg/kg
Reporting group description:	
Subjects received intravenous (IV) infusion of atezolizumab <=1 milligrams per kilogram (mg/kg) every 3 weeks (q3w) until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 3 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 3 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 10 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 10 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 15 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 20 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 20 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Expansion Cohort: Atezolizumab 1200 mg
Reporting group description:	
Subjects received IV infusion of atezolizumab 1200 mg q3w up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	

Reporting group values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg
Number of subjects	9	3	36
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	18
From 65-84 years	6	0	18
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	61.4	55.3	63.2

standard deviation	± 12.0	± 2.1	± 11.1

Gender categorical Units: Subjects			
Female	6	1	12
Male	3	2	24
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	8	2	35
Not Reported	0	0	0
Unkown	0	0	1
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	1	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
White	8	3	34
Other	0	0	0
Multiple	0	0	0

Reporting group values	Dose Escalation Cohort: Atezolizumab 15 mg/kg	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg
Number of subjects	236	146	228
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	137	82	151
From 65-84 years	97	63	77
85 years and over	2	1	0
Age continuous Units: years			
arithmetic mean	60.5	61.3	56.9
standard deviation	± 12.3	± 12.2	± 13.2
Gender categorical Units: Subjects			
Female	87	60	143
Male	149	86	85
Ethnicity Units: Subjects			
Hispanic or Latino	8	5	9

Not Hispanic or Latino	176	118	178
Not Reported	50	20	35
Unkown	2	3	6
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	5	3	9
Black or African American	4	8	12
Native Hawaiian or Other Pacific Islander	0	0	0
White	178	110	171
Other	49	25	34
Multiple	0	0	1

Reporting group values	Total		
Number of subjects	658		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	394		
From 65-84 years	261		
85 years and over	3		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	309		
Male	349		
Ethnicity			
Units: Subjects			
Hispanic or Latino	24		
Not Hispanic or Latino	517		
Not Reported	105		
Unkown	12		
Race			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	17		
Black or African American	27		
Native Hawaiian or Other Pacific Islander	0		
White	504		
Other	108		
Multiple	1		

End points reporting groups

Reporting group title	Dose Escalation Cohort: Atezolizumab <=1 mg/kg
Reporting group description:	
Subjects received intravenous (IV) infusion of atezolizumab <=1 milligrams per kilogram (mg/kg) every 3 weeks (q3w) until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 3 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 3 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 10 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 10 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 15 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Dose Escalation Cohort: Atezolizumab 20 mg/kg
Reporting group description:	
Subjects received IV infusion of atezolizumab 20 mg/kg q3w until DLT is reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Reporting group title	Expansion Cohort: Atezolizumab 1200 mg
Reporting group description:	
Subjects received IV infusion of atezolizumab 1200 mg q3w up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.	
Subject analysis set title	Safety-Evaluable Population: Atezolizumab
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety-Evaluable Population, defined as all enrolled subjects who received any amount of atezolizumab on study.	
Subject analysis set title	Baseline: ADA Positive Subjects
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who had a positive ADA result at baseline.	
Subject analysis set title	Post-Baseline: Treatment-Induced ADA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who had a baseline-negative ADA result who developed anti-drug antibodies at any time after initial drug administration.	
Subject analysis set title	Post-Baseline: Treatment-Enhanced ADA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who had a baseline-positive ADA result in whom the assay signal was enhanced at any time after initial drug administration.	
Subject analysis set title	PK Evaluable Population: Atezolizumab 0.01 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PK Evaluable Population, dose escalation cohort: subjects who received 0.01 mg/kg of atezolizumab.	

Subject analysis set title	PK Evaluable Population: Atezolizumab 0.03 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 0.03 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 0.1 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 0.1 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 0.3 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 0.3 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 1 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 1 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 3 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 3 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 10 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 10 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 15 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 15 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 20 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, dose escalation cohort: subjects who received 20 mg/kg of atezolizumab.

Subject analysis set title	PK Evaluable Population: Atezolizumab 1200 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK Evaluable Population, expansion cohort: subjects who received 1200 mg IV infusion of atezolizumab q3w up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurs first.

Subject analysis set title	Efficacy Evaluable Subjects: HR+Breast Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with HR+ breast cancer with measurable disease at baseline.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with bladder transitional cell carcinoma

Subject analysis set title	Efficacy Evaluable Subjects: Head and Neck Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with head and neck cancer.

Subject analysis set title	Efficacy evaluable subjects: Melanoma
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with melanoma

Subject analysis set title	Efficacy evaluable subjects: Non-Small Cell Lung Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with non-small cell lung cancer.

Subject analysis set title	Efficacy Evaluable Subjects: Prostate Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with prostate cancer.

Subject analysis set title	Efficacy Evaluable Subjects: Renal Cell Carcinoma
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with renal cell carcinoma.

Subject analysis set title	Efficacy Evaluable Subjects: Triple Negative Breast Cancer
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with triple negative breast cancer.

Subject analysis set title	Efficacy Evaluable Subjects: Tumor Types Where <20 subjects
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with tumor types where <20 subjects were enrolled.

Subject analysis set title	Efficacy Evaluable Subjects: HR+Breast Cancer IC0/1
Subject analysis set type	Safety analysis

Subject analysis set description:

Efficacy evaluable subject with HR+breast cancer IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: HR+Breast Cancer IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with HR+breast cancer IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: HR+Breast Cancer IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with HR+breast cancer IC0.

Subject analysis set title	Efficacy Evaluable Subjects: HR+Breast Cancer IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with HR+breast cancer IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with BTCC IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with BTCC IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC Unknown IC Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with BTCC unknown IC group.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with BTCC IC0.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with BTCC IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: BTCC Unknown IC Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with BTCC unknown IC group

Subject analysis set title	Efficacy Evaluable Subjects: Head and Neck Cancer IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with head and neck cancer IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: Head and Neck Cancer IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with head and neck cancer IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: Head and Neck Cancer IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with head and neck cancer IC0.

Subject analysis set title	Efficacy Evaluable Subjects: Head and Neck Cancer IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with head and neck cancer IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: Melanoma IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with melanoma IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: Melanoma IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with melanoma IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: Melanoma Unknown IC Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with melanoma unknown IC group.

Subject analysis set title	Efficacy Evaluable Subjects: Melanoma IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with melanoma IC0

Subject analysis set title	Efficacy Evaluable Subjects: Melanoma IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with melanoma IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC TC0/1/2 and IC0/1/2
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC TC0/1/2 and IC0/1/2.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC TC3 or IC3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC TC3 or IC3.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC Unkown TC or IC Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC unknown TC or IC group.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC IC0.

Subject analysis set title	Efficacy Evaluable Subjects: NSCLC IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with NSCLC IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: Prostate Cancer IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with prostate cancer IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: Prostate Cancer Unkown IC Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with prostate cancer unknown IC group.

Subject analysis set title	Efficacy Evaluable Subjects: Prostate Cancer IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with prostate cancer IC0.

Subject analysis set title	Efficacy Evaluable Subjects: Prostate Cancer IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with prostate cancer IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: RCC IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with RCC IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: RCC IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with RCC IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: RCC IC Group Unknown
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Efficacy evaluable subjects with RCC IC group unknown.

Subject analysis set title	Efficacy Evaluable Subjects: RCC IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with RCC IC0.

Subject analysis set title	Efficacy Evaluable Subjects: RCC IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with RCC IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: TNBC IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with TNBC IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: TNBC IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with TNBC IC2/3.

Subject analysis set title	Efficacy Evaluable Subjects: TNBC IC Group Unknown
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with TNBC IC group unknown.

Subject analysis set title	Efficacy Evaluable Subjects: TNBC IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with TNBC IC0.

Subject analysis set title	Efficacy Evaluable Subjects: TNBC IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with TNBC IC1/2/3.

Subject analysis set title	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC0/1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with tumor types where <20 subjects enrolled IC0/1.

Subject analysis set title	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with tumor types where <20 subjects enrolled IC2/3.

Subject analysis set title	Efficacy Evaluable: Tumor Types <20 Subjects IC Group Unknown
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with tumor types where <20 subjects enrolled IC group unknown.

Subject analysis set title	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC0
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with tumor types <20 subjects enrolled IC0.

Subject analysis set title	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC1/2/3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Efficacy evaluable subjects with tumor types where <20 Subjects Enrolled IC1/2/3.

Primary: Number of Subjects With Dose Limiting Toxicities (DLTs)

End point title	Number of Subjects With Dose Limiting Toxicities (DLTs)[1]

End point description:

End point type	Primary

End point timeframe:

Day 1 up to Day 21

Notes:

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

End point values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	3	36	236
Units: Number of Subjects	0	0	0	0

End point values	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	228		
Units: Number of Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Tolerated Dose (MTD) or Maximum Administered Dose (MAD) of Atezolizumab

End point title	Maximum Tolerated Dose (MTD) or Maximum Administered Dose (MAD) of Atezolizumab[2][3]

End point description:

Maximum administered dose of atezolizumab in the safety-evaluable population.

End point type	Primary

End point timeframe:

Day 1 up to Day 21

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: No statistical analyses for this end point.

[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: No statistical analyses for this end point.

End point values	Expansion Cohort: Atezolizumab 1200 mg			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: mg	1200			

Statistical analyses

No statistical analyses for this end point

Primary: Recommended Phase 2 Dose (RP2D) of Atezolizumab

End point title	Recommended Phase 2 Dose (RP2D) of Atezolizumab[4]

End point description:

End point type	Primary

End point timeframe:

Baseline up to time of determination of MTD (up to Day 21)

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: No statistical analyses for this end point.

End point values	Safety-Evaluable Population: Atezolizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	658			
Units: mg	1200			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events

End point title	Percentage of Subjects With Adverse Events[5]

End point description:

Percentage of subjects with adverse events in safety evaluable population, defined as all enrolled patients who received any amount of atezolizumab on study.

End point type	Primary

End point timeframe:

Baseline up to 90 days after the last dose of study treatment or until initiation of another anti-cancer therapy, whichever occurs first (up to approximately [approx] 7 years [yrs])

Notes:

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

End point values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	3	36	236
Units: Percentage of subjects				
number (not applicable)	100	100	97.2	98.3

End point values	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	228		
Units: Percentage of subjects				
number (not applicable)	99.3	98.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Therapeutic Antibodies (ATAs)

End point title	Number of Subjects With Anti-Therapeutic Antibodies (ATAs)

End point description:

End point type	Secondary

End point timeframe:

Predose up to 120 days after last dose of study treatment until death/study closure (up to approximately 7 years)

End point values	Baseline: ADA Positive Subjects	Post-Baseline: Treatment-Induced ADA	Post-Baseline: Treatment-Enhanced ADA	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	638	609	609	
Units: Subjects				
number (not applicable)	16	168	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve (AUC) 0-21 of Atezolizumab

End point title	Area Under the Concentration-Time Curve (AUC) 0-21 of Atezolizumab

End point description:

AUC from Day 1 to Day 21 in cycle 1, following multiple doses of atezolizumab given every 3 weeks by dose group in PK-evaluable population. Note: 888888 = not calculated.

End point type	Secondary

End point timeframe:

Cycle 1

End point values	PK Evaluable Population: Atezolizumab 0.1 mg/kg	PK Evaluable Population: Atezolizumab 0.3 mg/kg	PK Evaluable Population: Atezolizumab 1 mg/kg	PK Evaluable Population: Atezolizumab 3 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	3	3	3
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	1.62 (± 888888)	31.5 (± 8.1)	201 (± 8.5)	601 (± 34)

End point values	PK Evaluable Population: Atezolizumab 10 mg/kg	PK Evaluable Population: Atezolizumab 15 mg/kg	PK Evaluable Population: Atezolizumab 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	29	32	
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	2240 (± 17)	2730 (± 27)	3870 (± 21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Serum Concentration (Cmax) of Atezolizumab

End point description:

Cmax in cycle 1, following multiple IV doses of atezolizumab given every 3 weeks by dose group in PK-evaluable population.

End point type	Secondary

End point timeframe:

Cycle 1

End point values	PK Evaluable Population: Atezolizumab 0.01 mg/kg	PK Evaluable Population: Atezolizumab 0.03 mg/kg	PK Evaluable Population: Atezolizumab 0.1 mg/kg	PK Evaluable Population: Atezolizumab 0.3 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[6]	1[7]	1[8]	3
Units: ug/mL				
geometric mean (geometric coefficient of variation)	()	0.37 (± 888888)	0.96 (± 888888)	6.57 (± 1.33)

Notes:

[6] - Cmax not available due to insufficient data.

[7] - 888888 = not calculated.

[8] - 888888 = not calculated.

End point values	PK Evaluable Population: Atezolizumab 1 mg/kg	PK Evaluable Population: Atezolizumab 3 mg/kg	PK Evaluable Population: Atezolizumab 10 mg/kg	PK Evaluable Population: Atezolizumab 15 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	35	228
Units: ug/mL				
geometric mean (geometric coefficient of variation)	23.40 (± 8.55)	77.30 (± 19.9)	255 (± 51.0)	372 (± 199)

End point values	PK Evaluable Population: Atezolizumab 20 mg/kg	PK Evaluable Population: Atezolizumab 1200 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	131	194		
Units: ug/mL				
geometric mean (geometric coefficient of variation)	506 (± 115)	415 (± 107)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Serum Concentration (Cmin) of Atezolizumab

End point description:

Cmin in Cycle 1, following multiple IV doses of atezolizumab given every 3 weeks by dose group in PK-evaluable population.

End point type	Secondary

End point timeframe:

Cycle 1

End point values	PK Evaluable Population: Atezolizumab 0.01 mg/kg	PK Evaluable Population: Atezolizumab 0.03 mg/kg	PK Evaluable Population: Atezolizumab 0.1 mg/kg	PK Evaluable Population: Atezolizumab 0.3 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[9]	0[10]	0[11]	0[12]
Units: ug/mL				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[9] - Cmin is not available due to insufficient data.

[10] - .Cmin is not available due to insufficient data.

[11] - Cmin is not available due to insufficient data.

[12] - Cmin is not available due to insufficient data.

End point values	PK Evaluable Population: Atezolizumab 1 mg/kg	PK Evaluable Population: Atezolizumab 3 mg/kg	PK Evaluable Population: Atezolizumab 10 mg/kg	PK Evaluable Population: Atezolizumab 15 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	34	214
Units: ug/mL				
geometric mean (geometric coefficient of variation)	3.80 (± 160)	12.20 (± 62)	54.10 (± 25)	67.10 (± 73)

End point values	PK Evaluable Population: Atezolizumab 20 mg/kg	PK Evaluable Population: Atezolizumab 1200 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	132	30		
Units: ug/mL				
geometric mean (geometric coefficient of variation)	91.10 (± 36)	95.50 (± 51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) of Atezolizumab

End point title	Clearance (CL) of Atezolizumab

End point description:

CL in cycle 1, following multiple IV doses of atezolizumab given every 3 weeks by dose group in PK-evaluable population. Estimates are considered to be approximate in nature given the 18.0-26.6 day t1/2 and the fact that AUC0-inf was calculated using Cycle 1 data only. Note: 888888 = not calculated.

End point type	Secondary

End point timeframe:

Cycle 1

End point values	PK Evaluable Population: Atezolizumab 0.1 mg/kg	PK Evaluable Population: Atezolizumab 0.3 mg/kg	PK Evaluable Population: Atezolizumab 1 mg/kg	PK Evaluable Population: Atezolizumab 3 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	2	2	2
Units: L/day				
geometric mean (geometric coefficient of variation)	4.23 (± 888888)	0.603 (± 888888)	0.296 (± 888888)	0.420 (± 888888)

End point values	PK Evaluable Population: Atezolizumab 10 mg/kg	PK Evaluable Population: Atezolizumab 15 mg/kg	PK Evaluable Population: Atezolizumab 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	17	10	
Units: L/day				
geometric mean (geometric coefficient of variation)	0.329 (± 33)	0.365 (± 23)	0.288 (± 30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Volume at Steady State (Vss) of Atezolizumab

End point title	Volume at Steady State (Vss) of Atezolizumab

End point description:

Vss in Cycle 1, following multiple IV doses of atezolizumab given every 3 weeks by dose group in PK-evaluable population. Estimates are considered to be approximate in nature given the 18.0-26.6 day t1/2 and the fact that AUC0-inf was calculated using Cycle 1 data only. Note: 888888 = not calculated.

End point type	Secondary

End point timeframe:

Cycle 1

End point values	PK Evaluable Population: Atezolizumab 0.1 mg/kg	PK Evaluable Population: Atezolizumab 0.3 mg/kg	PK Evaluable Population: Atezolizumab 1 mg/kg	PK Evaluable Population: Atezolizumab 3 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	2	2	2
Units: Liter				
geometric mean (geometric coefficient of variation)	5.30 (± 888888)	2.79 (± 888888)	2.66 (± 888888)	5.20 (± 888888)

End point values	PK Evaluable Population: Atezolizumab 10 mg/kg	PK Evaluable Population: Atezolizumab 15 mg/kg	PK Evaluable Population: Atezolizumab 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	17	10	
Units: Liter				
geometric mean (geometric coefficient of variation)	4.28 (± 39)	4.89 (± 22)	3.89 (± 30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Best Overall Response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD), Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

End point title	Percentage of Subjects With Best Overall Response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD), Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

End point description:

Percentage of subjects with best overall response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD) in efficacy evaluable subjects with measurable disease at baseline by tumor type and IC group. Note: 000000 = not calculated. 888888 = not calculated.

End point type	Secondary

End point timeframe:

From Baseline up to the first occurrence of progression or death, whichever occurs first (up to approx 7 yrs)

End point values	Efficacy Evaluable Subjects: HR+Breast Cancer IC0/1	Efficacy Evaluable Subjects: HR+Breast Cancer IC2/3	Efficacy Evaluable Subjects: HR+Breast Cancer IC0	Efficacy Evaluable Subjects: HR+Breast Cancer IC1/2/3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	5	11	9
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 21.80)	0 (0.00 to 52.18)	0 (0.00 to 28.49)	0 (0.00 to 33.63)
Partial Response (PR)	0 (0.00 to 21.80)	0 (0.00 to 52.18)	0 (0.00 to 28.49)	0 (0.00 to 33.63)
Stable Disease (SD)	26.7 (7.79 to 55.10)	0 (0.00 to 52.18)	18.2 (2.28 to 51.78)	22.2 (2.81 to 60.01)
Progressive Disease (PD)	60 (32.29 to 83.66)	100 (47.82 to 100.00)	72.7 (39.03 to 93.98)	66.7 (29.93 to 92.51)

Missing or unevaluable	13.3 (000000 to 888888)	0 (000000 to 888888)	9.1 (000000 to 888888)	11.1 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: BTCC IC0/1	Efficacy Evaluable Subjects: BTCC IC2/3	Efficacy Evaluable Subjects: BTCC Unknown IC Group	Efficacy Evaluable Subjects: BTCC IC0
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	22	25	18
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	6.3 (1.31 to 17.20)	18.2 (5.19 to 40.28)	12.0 (2.55 to 31.22)	5.6 (0.14 to 27.29)
Partial Response (PR)	16.7 (7.48 to 30.22)	18.2 (5.19 to 40.28)	12.0 (2.55 to 31.22)	11.1 (1.38 to 34.71)
Stable Disease (SD)	18.8 (8.95 to 32.63)	22.7 (7.82 to 45.37)	16.0 (4.54 to 36.08)	11.1 (1.38 to 34.71)
Progressive Disease (PD)	47.9 (33.29 to 62.81)	27.3 (10.73 to 50.22)	52.0 (31.31 to 72.20)	61.1 (35.75 to 82.70)
Missing or unevaluable	10.4 (000000 to 888888)	13.6 (000000 to 888888)	8.0 (000000 to 888888)	11.1 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: BTCC IC1/2/3	Efficacy Evaluable Subjects: BTCC Unknown IC Group	Efficacy Evaluable Subjects: Head and Neck Cancer IC0/1	Efficacy Evaluable Subjects: Head and Neck Cancer IC2/3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	25	7	25
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	11.5 (4.35 to 23.44)	12.0 (2.55 to 31.22)	0 (0.00 to 40.96)	0 (0.00 to 13.72)
Partial Response (PR)	19.2 (9.63 to 32.53)	12.0 (2.55 to 31.22)	14.3 (0.36 to 57.87)	24.0 (9.36 to 45.13)
Stable Disease (SD)	23.1 (12.53 to 36.84)	16.0 (4.54 to 36.08)	42.9 (9.90 to 81.59)	12.0 (2.55 to 31.22)
Progressive Disease (PD)	34.6 (21.97 to 49.09)	52.0 (31.31 to 72.20)	28.6 (3.67 to 70.96)	48.0 (27.80 to 68.69)
Missing or unevaluable	11.5 (000000 to 888888)	8.0 (000000 to 888888)	14.3 (000000 to 888888)	16.0 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: Head and Neck Cancer IC0	Efficacy Evaluable Subjects: Head and Neck Cancer IC1/2/3	Efficacy Evaluable Subjects: Melanoma IC0/1	Efficacy Evaluable Subjects: Melanoma IC2/3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	29	20	18
Units: Subjects				

number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 70.76)	0 (0.00 to 11.94)	10.0 (1.23 to 31.70)	11.1 (1.38 to 34.71)
Partial Response (PR)	33.3 (0.84 to 90.57)	20.7 (7.99 to 39.72)	20.0 (5.73 to 43.66)	22.2 (6.41 to 47.64)
Stable Disease (SD)	33.3 (0.84 to 90.57)	17.2 (5.85 to 35.77)	0 (0.00 to 16.84)	44.4 (21.53 to 69.24)
Progressive Disease (PD)	33.3 (0.84 to 90.57)	44.8 (26.45 to 64.31)	65.0 (40.78 to 84.61)	22.2 (6.41 to 47.64)
Missing or unevaluable	0 (000000 to 888888)	17.2 (000000 to 888888)	5.0 (000000 to 888888)	0 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: Melanoma Unknown IC Group	Efficacy Evaluable Subjects: Melanoma IC0	Efficacy Evaluable Subjects: Melanoma IC1/2/3	Efficacy Evaluable Subjects: NSCLC TC0/1/2 and IC0/1/2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	16	22	59
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 52.18)	0 (0.00 to 20.59)	18.2 (5.19 to 40.28)	1.7 (0.04 to 9.09)
Partial Response (PR)	20.0 (0.51 to 71.64)	18.8 (4.05 to 45.65)	22.7 (7.82 to 45.37)	13.6 (6.04 to 24.98)
Stable Disease (SD)	60.0 (14.66 to 94.73)	0 (0.00 to 20.59)	36.4 (17.20 to 59.34)	30.5 (19.19 to 43.87)
Progressive Disease (PD)	20.0 (0.51 to 71.64)	75.0 (47.62 to 92.73)	22.7 (7.82 to 45.37)	45.8 (32.72 to 59.25)
Missing or unevaluable	0 (000000 to 888888)	6.3 (000000 to 888888)	0 (000000 to 888888)	8.5 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: NSCLC TC3 or IC3	Efficacy Evaluable Subjects: NSCLC Unkown TC or IC Group	Efficacy Evaluable Subjects: NSCLC IC0/1	Efficacy Evaluable Subjects: NSCLC IC2/3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	8	43	38
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 15.44)	0 (0.00 to 36.94)	0 (0.00 to 8.22)	2.6 (0.07 to 13.81)
Partial Response (PR)	50.0 (28.22 to 71.78)	0 (0.00 to 36.94)	16.3 (6.81 to 30.70)	31.6 (17.50 to 48.65)
Stable Disease (SD)	9.1 (1.12 to 29.16)	62.5 (24.49 to 91.48)	32.6 (19.08 to 48.54)	15.8 (6.02 to 31.25)
Progressive Disease (PD)	40.9 (20.71 to 63.65)	37.5 (8.52 to 75.51)	44.2 (29.08 to 60.12)	44.7 (28.62 to 61.70)
Missing or unevaluable	0 (000000 to 888888)	0 (000000 to 888888)	7.0 (000000 to 888888)	5.3 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: NSCLC IC0	Efficacy Evaluable Subjects: NSCLC IC1/2/3	Efficacy Evaluable Subjects: Prostate Cancer IC0/1	Efficacy Evaluable Subjects: Prostate Cancer Unkown IC Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	53	33	2
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 12.34)	1.9 (0.05 to 10.07)	0 (0.00 to 14.25)	0 (0.00 to 97.50)
Partial Response (PR)	14.3 (4.03 to 32.67)	28.3 (16.79 to 42.35)	4.2 (0.11 to 21.12)	0 (0.00 to 97.50)
Stable Disease (SD)	42.9 (24.46 to 62.82)	15.1 (6.75 to 27.59)	25.0 (9.77 to 46.71)	100 (2.50 to 100.00)
Progressive Disease (PD)	35.7 (18.64 to 55.93)	49.1 (35.06 to 63.16)	62.5 (40.59 to 81.20)	0 (0.00 to 97.50)
Missing or unevaluable	7.1 (000000 to 888888)	5.7 (000000 to 888888)	8.3 (000000 to 888888)	0 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: Prostate Cancer IC0	Efficacy Evaluable Subjects: Prostate Cancer IC1/2/3	Efficacy Evaluable Subjects: RCC IC0/1	Efficacy Evaluable Subjects: RCC IC2/3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	5	38	25
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 17.65)	0 (0.00 to 52.18)	0 (0.00 to 9.25)	4.0 (0.10 to 20.35)
Partial Response (PR)	5.3 (0.13 to 26.03)	0 (0.00 to 52.18)	13.2 (4.41 to 28.09)	12.0 (2.55 to 31.22)
Stable Disease (SD)	21.1 (6.05 to 45.57)	40.0 (5.27 to 85.34)	47.4 (30.98 to 64.18)	40.0 (21.13 to 61.33)
Progressive Disease (PD)	68.4 (43.45 to 87.42)	40.0 (5.27 to 85.34)	31.6 (17.50 to 48.65)	44.0 (24.40 to 65.07)
Missing or unevaluable	5.3 (000000 to 888888)	20.0 (000000 to 888888)	7.9 (000000 to 888888)	0 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: RCC IC Group Unknown	Efficacy Evaluable Subjects: RCC IC0	Efficacy Evaluable Subjects: RCC IC1/2/3	Efficacy Evaluable Subjects: TNBC IC0/1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	22	41	38
Units: Subjects				
number (confidence interval 95%)				

Complete Response (CR)	0 (0.00 to 33.63)	0 (0.00 to 15.44)	2.4 (0.06 to 12.86)	0 (0.00 to 9.49)
Partial Response (PR)	11.1 (0.28 to 48.25)	9.1 (1.12 to 29.16)	14.6 (5.57 to 29.17)	5.4 (0.66 to 18.19)
Stable Disease (SD)	66.7 (29.93 to 92.51)	45.5 (24.39 to 67.79)	43.9 (28.47 to 60.25)	10.8 (3.03 to 25.42)
Progressive Disease (PD)	22.2 (2.81 to 60.01)	36.4 (17.20 to 59.34)	36.6 (22.12 to 53.06)	70.3 (53.02 to 84.13)
Missing or unevaluable	0 (000000 to 888888)	9.1 (000000 to 888888)	2.4 (000000 to 888888)	13.5 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: TNBC IC2/3	Efficacy Evaluable Subjects: TNBC IC Group Unknown	Efficacy Evaluable Subjects: TNBC IC0	Efficacy Evaluable Subjects: TNBC IC1/2/3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	74	4	21	91
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	6.8 (2.23 to 15.07)	0 (0.00 to 60.24)	0 (0.00 to 16.84)	5.5 (1.81 to 12.36)
Partial Response (PR)	5.4 (1.49 to 13.27)	0 (0.00 to 60.24)	0 (0.00 to 16.84)	6.6 (2.46 to 13.80)
Stable Disease (SD)	13.5 (6.68 to 23.45)	25.0 (0.63 to 80.59)	15.0 (3.21 to 37.89)	12.1 (6.19 to 20.60)
Progressive Disease (PD)	60.8 (48.77 to 71.96)	50.0 (6.76 to 93.24)	80.0 (56.34 to 94.27)	60.4 (49.64 to 70.54)
Missing or unevaluable	13.5 (000000 to 888888)	25.0 (000000 to 888888)	5.0 (000000 to 888888)	51.4 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC0/1	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC2/3	Efficacy Evaluable: Tumor Types <20 Subjects IC Group Unknown	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC0
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	68	15	45
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	0 (0.00 to 5.60)	1.5 (0.04 to 8.04)	0 (0.00 to 33.63)	0 (0.00 to 8.41)
Partial Response (PR)	1.6 (0.04 to 8.40)	6.0 (1.65 to 14.59)	0 (0.00 to 33.63)	0 (0.00 to 8.41)
Stable Disease (SD)	14.1 (6.64 to 25.02)	22.4 (13.11 to 34.22)	0 (0.00 to 33.63)	11.9 (3.98 to 25.63)
Progressive Disease (PD)	53.1 (40.23 to 65.72)	53.7 (41.12 to 66.00)	77.8 (39.99 to 97.19)	52.4 (36.42 to 68.00)
Missing or unevaluable	31.3 (000000 to 888888)	16.4 (000000 to 888888)	22.2 (000000 to 888888)	35.7 (000000 to 888888)

End point values	Efficacy Evaluable Subjects: Tumor Types <20 Subjects IC1/2/3			
Subject group type	Subject analysis set			
Number of subjects analysed	90			
Units: Subjects				
number (confidence interval 95%)				
Complete Response (CR)	1.1 (0.03 to 6.10)			
Partial Response (PR)	5.6 (1.85 to 12.63)			
Stable Disease (SD)	21.3 (13.37 to 331.31)			
Progressive Disease (PD)	53.9 (43.04 to 64.56)			
Missing or unevaluable	18.0 (000000 to 888888)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Best Overall Response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD), Assessed by Immune-Related Response Criteria (irRC)

End point title	Percentage of Subjects With Best Overall Response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD), Assessed by Immune-Related Response Criteria (irRC)

End point description:

End point type	Secondary

End point timeframe:

From Baseline up to the first occurrence of progression or death, whichever occurs first (up to approx 7 yrs)

End point values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[13]	0[14]	0[15]	0[16]
Units: Subjects				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[13] - This outcome measure is not being evaluated.

[14] - This outcome measure is not being evaluated.

[15] - This outcome measure is not being evaluated.

[16] - This outcome measure is not being evaluated.

End point values	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[17]	0[18]		
Units: Subjects				
number (confidence interval 95%)	(to)	(to)		

Notes:

[17] - This outcome measure is not being evaluated.

[18] - This outcome measure is not being evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Objective Response (Complete Response [CR] or Partial Response [PR]), Assessed by RECIST v1.1

End point title	Number of Subjects With Objective Response (Complete Response [CR] or Partial Response [PR]), Assessed by RECIST v1.1

End point description:

Objective Response (Complete Response [CR] or Partial Response [PR]) in efficacy evaluable population.

End point type	Secondary

End point timeframe:

From Baseline up to the first occurrence of progression or death, whichever occurs first (up to approx 7 yrs)

End point values	Efficacy Evaluable Subjects: HR+Breast Cancer	Efficacy Evaluable Subjects: BTCC	Efficacy Evaluable Subjects: Head and Neck Cancer	Efficacy evaluable subjects: Melanoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	95	32	43
Units: Subjects				
number (not applicable)				
Complete Response (CR)	0	10	0	4
Partial Response (PR)	0	15	7	9

End point values	Efficacy evaluable subjects: Non-Small Cell Lung	Efficacy Evaluable Subjects: Prostate	Efficacy Evaluable Subjects: Renal Cell	Efficacy Evaluable Subjects: Triple Negative

	Cancer	Cancer	Carcinoma	Breast Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	89	25	72	115
Units: Subjects				
number (not applicable)				
Complete Response (CR)	1	0	1	5
Partial Response (PR)	19	1	9	6

End point values	Efficacy Evaluable Subjects: Tumor Types Where <20 subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	150			
Units: Subjects				
number (not applicable)				
Complete Response (CR)	1			
Partial Response (PR)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response (CR or PR), Assessed by irRC

End point title	Percentage of Participants With Objective Response (CR or PR), Assessed by irRC

End point description:

End point type	Secondary

End point timeframe:

From Baseline up to the first occurrence of progression or death, whichever occurs first (up to approx 7 yrs)

End point values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[19]	0[20]	0[21]	0[22]
Units: Participants				
number (not applicable)				

Notes:

[19] - This outcome measure is not being evaluated.

[20] - This outcome measure is not being evaluated.

[21] - This outcome measure is not being evaluated.

[22] - This outcome measure is not being evaluated.

End point values	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[23]	0[24]		
Units: Participants				
number (not applicable)				

Notes:

[23] - This outcome measure is not being evaluated.

[24] - This outcome measure is not being evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response, Assessed by RECIST v1.1

End point title	Duration of Objective Response, Assessed by RECIST v1.1

End point description:

Duration of objective response in efficacy evaluable population. Note: 999999= not available.

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented objective response to the time of relapse or death from any cause (up to approx 7 yrs)

End point values	Efficacy Evaluable Subjects: HR+Breast Cancer	Efficacy Evaluable Subjects: BTCC	Efficacy Evaluable Subjects: Head and Neck Cancer	Efficacy evaluable subjects: Melanoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	95	32	43
Units: Months				
number (not applicable)	999999	22.11	7.36	62.39

End point values	Efficacy evaluable subjects: Non-Small Cell Lung Cancer	Efficacy Evaluable Subjects: Prostate Cancer	Efficacy Evaluable Subjects: Renal Cell Carcinoma	Efficacy Evaluable Subjects: Triple Negative Breast Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	89	25	72	115
Units: Months				

number (not applicable)	16.38	7.23	13.09	21.06

End point values	Efficacy Evaluable Subjects: Tumor Types Where <20 subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	150			
Units: Months				
number (not applicable)	7.69			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response, Assessed by irRC

End point title	Duration of Objective Response, Assessed by irRC

End point description:

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented objective response to the time of relapse or death from any cause (up to approx 7 yrs)

End point values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[25]	0[26]	0[27]	0[28]
Units: Months				
number (not applicable)				

Notes:

[25] - This outcome measure is not being evaluated.

[26] - This outcome measure is not being evaluated.

[27] - This outcome measure is not being evaluated.

[28] - This outcome measure is not being evaluated.

End point values	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[29]	0[30]		

Units: Months				
number (not applicable)				

Notes:

[29] - This outcome measure is not being evaluated.

[30] - This outcome measure is not being evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS), Assessed by RECIST v1.1

End point title	Progression-Free Survival (PFS), Assessed by RECIST v1.1

End point description:

Progression-free survival in efficacy evaluable population.

End point type	Secondary

End point timeframe:

From Baseline up to the first occurrence of progression or death, whichever occurs first (up to approx 7 yrs)

End point values	Efficacy Evaluable Subjects: HR+Breast Cancer	Efficacy Evaluable Subjects: BTCC	Efficacy Evaluable Subjects: Head and Neck Cancer	Efficacy evaluable subjects: Melanoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	95	32	43
Units: Months				
number (not applicable)	1.40	2.66	2.64	4.17

End point values	Efficacy evaluable subjects: Non-Small Cell Lung Cancer	Efficacy Evaluable Subjects: Prostate Cancer	Efficacy Evaluable Subjects: Renal Cell Carcinoma	Efficacy Evaluable Subjects: Triple Negative Breast Cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	89	25	72	115
Units: Months				
number (not applicable)	3.02	3.14	5.39	1.40

End point values	Efficacy Evaluable Subjects: Tumor Types Where <20 subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	150			

Units: Months				
number (not applicable)	2.50			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS, Assessed by irRC

End point title	PFS, Assessed by irRC

End point description:

End point type	Secondary

End point timeframe:

From Baseline up to the first occurrence of progression or death, whichever occurs first (up to approx 7 yrs)

End point values	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg	Dose Escalation Cohort: Atezolizumab 15 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[31]	0[32]	0[33]	0[34]
Units: Months				
number (not applicable)				

Notes:

[31] - This outcome measure is not being evaluated.

[32] - This outcome measure is not being evaluated.

[33] - This outcome measure is not being evaluated.

[34] - This outcome measure is not being evaluated.

End point values	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[35]	0[36]		
Units: Months				
number (not applicable)				

Notes:

[35] - This outcome measure is not being evaluated.

[36] - This outcome measure is not being evaluated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug administration to the data cutoff date: 30 September 2018.

Adverse event reporting additional description:

Includes safety evaluable population, defined as all enrolled patients who received any amount of atezolizumab on study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Dose Escalation Cohort: Atezolizumab <=1 mg/kg

Reporting group description:

Subjects received IV infusion of atezolizumab <=1 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurred first.

Reporting group title	Dose Escalation Cohort: Atezolizumab 3 mg/kg

Reporting group description:

Subjects received IV infusion of atezolizumab 3 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurred first.

Reporting group title	Dose Escalation Cohort: Atezolizumab 10 mg/kg

Reporting group description:

Subjects received IV infusion of atezolizumab 10 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurred first.

Reporting group title	Dose Escalation Cohort: Atezolizumab 15 mg/kg

Reporting group description:

Subjects received IV infusion of atezolizumab 15 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurred first.

Reporting group title	Dose Escalation Cohort: Atezolizumab 20 mg/kg

Reporting group description:

Subjects received IV infusion of atezolizumab 20 mg/kg q3w until DLT was reached or up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurred first.

Reporting group title	Expansion Cohort: Atezolizumab 1200 mg

Reporting group description:

Subjects received IV infusion of atezolizumab 1200 mg q3w up to end of study or treatment discontinuation or death or until initiation of another anti cancer therapy, whichever occurred first.

Serious adverse events	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	20 / 36 (55.56%)
number of deaths (all causes)	1	0	13
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 melanoma in situ			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 neoplasm progression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Transitional cell carcinoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
Arterial thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 compression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 like illness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 necrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
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 hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 arrest			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alphavirus test positive			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 bilirubin increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
Ankle fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis radiation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urostomy complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 dehiscence			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 myocardial infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 tamponade			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
Ataxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 mass			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological symptom			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 cord compression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vith nerve disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 adhesions			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 distension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 colitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
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			
Autoimmune hepatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder rupture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 pruritic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 bladder haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 retenion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 hypothyroidism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
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 pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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			
Appendicitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (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
Arthritis infective			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 ulcerative gingivostomatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia influenzal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (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
Urosepsis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 device infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumor lysis syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
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	Dose Escalation Cohort: Atezolizumab 15 mg/kg	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	115 / 236 (48.73%)	65 / 146 (44.52%)	103 / 228 (45.18%)
number of deaths (all causes)	85	39	181
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Infected neoplasm			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
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	1 / 236 (0.42%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	3 / 236 (1.27%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial thrombosis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	0 / 228 (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
Haematoma			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular compression			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Fatigue			
subjects affected / exposed	5 / 236 (2.12%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	2 / 5	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Influenza like illness			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			

subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Malaise			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Oedema peripheral			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Pain			
subjects affected / exposed	3 / 236 (1.27%)	3 / 146 (2.05%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 3	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	0 / 228 (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
Pyrexia			
subjects affected / exposed	9 / 236 (3.81%)	4 / 146 (2.74%)	6 / 228 (2.63%)
occurrences causally related to treatment / all	7 / 9	2 / 4	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			

subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Reproductive system and breast disorders			
Breast necrosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Aspiration			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Chronic obstructive pulmonary disorder			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			

subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	7 / 236 (2.97%)	9 / 146 (6.16%)	8 / 228 (3.51%)
occurrences causally related to treatment / all	0 / 7	3 / 13	2 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
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	4 / 236 (1.69%)	4 / 146 (2.74%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	2 / 4	3 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Obstructive airways disorder			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 236 (0.42%)	4 / 146 (2.74%)	5 / 228 (2.19%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 236 (0.42%)	2 / 146 (1.37%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
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	2 / 236 (0.85%)	2 / 146 (1.37%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pulmonary oedema			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	5 / 228 (2.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
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			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Alphavirus test positive			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood bilirubin increased			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Liver function test increased			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Cystitis radiation			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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

Femur fracture			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Head injury			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Urostomy complication			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound complication			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Arrhythmia			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	2 / 236 (0.85%)	2 / 146 (1.37%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	0 / 228 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Pericardial effusion			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			

subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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 disorders			
Ataxia			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Brain oedema			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Encephalopathy			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Epilepsy			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Focal dyscognitive seizures			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
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 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial mass			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Neurological symptom			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
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 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vith nerve disorder			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 236 (1.69%)	2 / 146 (1.37%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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 distension			

subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	4 / 236 (1.69%)	4 / 146 (2.74%)	4 / 228 (1.75%)
occurrences causally related to treatment / all	0 / 4	1 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	0 / 228 (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
Ascites			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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 colitis			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	3 / 228 (1.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			

subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
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 haemorrhage			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
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	2 / 236 (0.85%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Vomiting			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Bile duct obstruction			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder rupture			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hepatic haematoma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Rash			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pruritic			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	4 / 236 (1.69%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
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	4 / 236 (1.69%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Ureteric obstruction			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder haemorrhage			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retenion			

subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	0 / 228 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hypothyroidism			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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 / 236 (0.00%)	1 / 146 (0.68%)	3 / 228 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
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	5 / 236 (2.12%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 236 (0.42%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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

Flank pain			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	3 / 228 (1.32%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Pain in extremity			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	0 / 228 (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
Rotator cuff syndrome			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Atypical pneumonia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Biliary tract infection			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	5 / 236 (2.12%)	0 / 146 (0.00%)	4 / 228 (1.75%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	0 / 228 (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
Empyema			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Erysipelas			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			

subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising ulcerative gingivostomatitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 236 (1.69%)	2 / 146 (1.37%)	3 / 228 (1.32%)
occurrences causally related to treatment / all	1 / 4	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Pyelonephritis			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	0 / 228 (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
Pyelonephritis acute			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	4 / 236 (1.69%)	0 / 146 (0.00%)	4 / 228 (1.75%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Septic shock			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	6 / 236 (2.54%)	1 / 146 (0.68%)	5 / 228 (2.19%)
occurrences causally related to treatment / all	1 / 6	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	3 / 236 (1.27%)	1 / 146 (0.68%)	6 / 228 (2.63%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (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
Failure to thrive			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
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	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	4 / 228 (1.75%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			

subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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
Tumor lysis syndrome			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (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

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

Non-serious adverse events	Dose Escalation Cohort: Atezolizumab <=1 mg/kg	Dose Escalation Cohort: Atezolizumab 3 mg/kg	Dose Escalation Cohort: Atezolizumab 10 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	3 / 3 (100.00%)	35 / 36 (97.22%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Malignant melanoma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Melanocytic naevus			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic keratosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Skin papilloma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Tumour haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Tumour necrosis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Tumour ulceration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	2	1
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Chest discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	2	0	5
Chills			
subjects affected / exposed	4 / 9 (44.44%)	3 / 3 (100.00%)	5 / 36 (13.89%)
occurrences (all)	6	3	10
Fatigue			
subjects affected / exposed	7 / 9 (77.78%)	3 / 3 (100.00%)	18 / 36 (50.00%)
occurrences (all)	17	3	35
Hernia pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	6 / 36 (16.67%)
occurrences (all)	0	0	9
Mucosal Inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Nodule			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	3	0	2
Oedema peripheral			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	9 / 36 (25.00%)
occurrences (all)	3	1	12
Pain			
subjects affected / exposed	4 / 9 (44.44%)	1 / 3 (33.33%)	4 / 36 (11.11%)
occurrences (all)	5	1	4
Pyrexia			
subjects affected / exposed	4 / 9 (44.44%)	3 / 3 (100.00%)	9 / 36 (25.00%)
occurrences (all)	6	3	16
Temperature intolerance			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	5 / 36 (13.89%)
occurrences (all)	1	0	6
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Breast tenderness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Vaginal mucosal blistering			

subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	3 / 9 (33.33%)	3 / 3 (100.00%)	9 / 36 (25.00%)
occurrences (all)	3	5	14
Dyspnoea			
subjects affected / exposed	4 / 9 (44.44%)	1 / 3 (33.33%)	13 / 36 (36.11%)
occurrences (all)	7	1	25
Dyspnoea exertional			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	4 / 36 (11.11%)
occurrences (all)	0	1	4
Nasal congestion			
subjects affected / exposed	2 / 9 (22.22%)	2 / 3 (66.67%)	4 / 36 (11.11%)
occurrences (all)	2	2	7
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	7 / 36 (19.44%)
occurrences (all)	1	0	7
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Pneumonitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Productive cough			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	5 / 36 (13.89%)
occurrences (all)	2	0	9
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Rhinitis allergic			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	4
Sinus congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	5 / 36 (13.89%)
occurrences (all)	0	0	5
Sinus disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Upper airway cough syndrome			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	1	0	6
Wheezing			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	3 / 36 (8.33%)
occurrences (all)	0	1	5
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	6 / 36 (16.67%)
occurrences (all)	6	1	7
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Insomnia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	11 / 36 (30.56%)
occurrences (all)	2	1	12
Product issues			
Device occlusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Bleeding time prolonged			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Body temperature increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Platelet count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Weight increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Fall			

subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Muscle strain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Splinter			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Tendon rupture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Wound complication			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	2	0	2
Palpitations			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	3
Sinus Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	9 / 36 (25.00%)
occurrences (all)	3	1	11
Dysgeusia			

subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	4	0	2
Headache			
subjects affected / exposed	3 / 9 (33.33%)	1 / 3 (33.33%)	14 / 36 (38.89%)
occurrences (all)	4	2	24
Hypoesthesia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	2	0	3
Neuropathy peripheral			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	0	0	4
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Sciatica			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	6 / 36 (16.67%)
occurrences (all)	2	0	20
Anaemia Macrocytic			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1

Ear and labyrinth disorders			
Ear Congestion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Ear Discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Ear Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Eye disorders			
Altered visual depth perception			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Eye Pruritus			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Lacrimation increased			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	2	1	1
Ulcerative keratitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Vitreous floaters			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	1	0	3
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			

subjects affected / exposed	3 / 9 (33.33%)	0 / 3 (0.00%)	8 / 36 (22.22%)
occurrences (all)	3	0	9
Abdominal pain upper			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	2	0	4
Constipation			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	9 / 36 (25.00%)
occurrences (all)	3	1	11
Diarrhoea			
subjects affected / exposed	5 / 9 (55.56%)	0 / 3 (0.00%)	18 / 36 (50.00%)
occurrences (all)	12	0	36
Dry mouth			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Dysphagia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Frequent bowl movements			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	2 / 36 (5.56%)
occurrences (all)	3	1	3
Haemorrhoids			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Hypoaesthesia oral			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Loose tooth			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	7 / 9 (77.78%)	2 / 3 (66.67%)	10 / 36 (27.78%)
occurrences (all)	9	2	17
Oesophagitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Oral pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Retching			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)	1 / 3 (33.33%)	7 / 36 (19.44%)
occurrences (all)	2	1	8
Salvary gland enlargement			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Dry skin			
subjects affected / exposed	1 / 9 (11.11%)	1 / 3 (33.33%)	2 / 36 (5.56%)
occurrences (all)	1	1	3

Erythema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	2 / 36 (5.56%)
occurrences (all)	0	2	2
Hyperhidrosis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	4	0	2
Hyperkeratosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Madarosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	2 / 9 (22.22%)	3 / 3 (100.00%)	3 / 36 (8.33%)
occurrences (all)	3	3	3
Pruritus			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	10 / 36 (27.78%)
occurrences (all)	2	1	17
Pruritus generalised			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	1 / 9 (11.11%)	2 / 3 (66.67%)	9 / 36 (25.00%)
occurrences (all)	2	2	12
Rash maculo-papular			
subjects affected / exposed	1 / 9 (11.11%)	1 / 3 (33.33%)	4 / 36 (11.11%)
occurrences (all)	1	2	5
Rash pruritic			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Rash vesicular			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0

Transient acantholytic dermatosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Vitiligo			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 9 (0.00%)	2 / 3 (66.67%)	3 / 36 (8.33%)
occurrences (all)	0	2	3
Nocturia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Pollakiuria			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	2	0	4
Proteinuria			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Urethral obstruction			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	0	0	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 9 (33.33%)	1 / 3 (33.33%)	10 / 36 (27.78%)
occurrences (all)	4	2	18
Arthritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Back pain			
subjects affected / exposed	2 / 9 (22.22%)	1 / 3 (33.33%)	10 / 36 (27.78%)
occurrences (all)	2	1	12

Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Chrondrosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	2	0	6
Joint swelling			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	3
Muscular weakness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	1	0	6
Musculoskeletal chest pain			
subjects affected / exposed	1 / 9 (11.11%)	1 / 3 (33.33%)	4 / 36 (11.11%)
occurrences (all)	1	1	5
Musculoskeletal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	8 / 36 (22.22%)
occurrences (all)	0	0	11
Myalgia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	4	0	4
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	0	0	4
Osteoarthritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	3 / 9 (33.33%)	0 / 3 (0.00%)	6 / 36 (16.67%)
occurrences (all)	5	0	7

Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	2	2	1
Candida infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Ear infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Fungal infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	2	0	2
Herpes Zoster			
subjects affected / exposed	1 / 9 (11.11%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Localised infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	1 / 36 (2.78%)
occurrences (all)	0	1	2
Lung infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	3
Nail bed infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Tooth abscess			

subjects affected / exposed	1 / 9 (11.11%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 9 (33.33%)	2 / 3 (66.67%)	6 / 36 (16.67%)
occurrences (all)	8	4	6
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	4 / 36 (11.11%)
occurrences (all)	0	0	7
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 9 (33.33%)	1 / 3 (33.33%)	10 / 36 (27.78%)
occurrences (all)	3	1	13
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	5 / 36 (13.89%)
occurrences (all)	0	0	6
Hypercalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	6 / 36 (16.67%)
occurrences (all)	0	1	12
Hyperkalaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Hyperuricaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 3 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Hypomagnesaemia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 3 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	7
Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 3 (33.33%)	2 / 36 (5.56%)
occurrences (all)	0	4	3

Non-serious adverse events	Dose Escalation Cohort: Atezolizumab 15 mg/kg	Dose Escalation Cohort: Atezolizumab 20 mg/kg	Expansion Cohort: Atezolizumab 1200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	219 / 236 (92.80%)	143 / 146 (97.95%)	207 / 228 (90.79%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	1	1	0
Malignant melanoma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Melanocytic naevus			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic keratosis			
subjects affected / exposed	4 / 236 (1.69%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	5	0	0
Skin papilloma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Tumour haemorrhage			
subjects affected / exposed	4 / 236 (1.69%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences (all)	4	0	1
Tumour necrosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	4 / 236 (1.69%)	10 / 146 (6.85%)	1 / 228 (0.44%)
occurrences (all)	6	10	1
Tumour ulceration			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hot flush			

subjects affected / exposed	4 / 236 (1.69%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences (all)	4	3	1
Hypertension			
subjects affected / exposed	11 / 236 (4.66%)	6 / 146 (4.11%)	11 / 228 (4.82%)
occurrences (all)	12	8	16
Hypotension			
subjects affected / exposed	10 / 236 (4.24%)	8 / 146 (5.48%)	4 / 228 (1.75%)
occurrences (all)	10	8	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	47 / 236 (19.92%)	28 / 146 (19.18%)	27 / 228 (11.84%)
occurrences (all)	72	62	40
Chest discomfort			
subjects affected / exposed	4 / 236 (1.69%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences (all)	4	4	1
Chills			
subjects affected / exposed	26 / 236 (11.02%)	19 / 146 (13.01%)	11 / 228 (4.82%)
occurrences (all)	27	22	12
Fatigue			
subjects affected / exposed	98 / 236 (41.53%)	56 / 146 (38.36%)	88 / 228 (38.60%)
occurrences (all)	151	78	122
Hernia pain			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	1	1	0
Influenza like illness			
subjects affected / exposed	13 / 236 (5.51%)	18 / 146 (12.33%)	11 / 228 (4.82%)
occurrences (all)	19	22	12
Mucosal Inflammation			
subjects affected / exposed	7 / 236 (2.97%)	4 / 146 (2.74%)	1 / 228 (0.44%)
occurrences (all)	9	5	1
Nodule			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			

subjects affected / exposed	1 / 236 (0.42%)	5 / 146 (3.42%)	2 / 228 (0.88%)
occurrences (all)	1	5	2
Oedema peripheral			
subjects affected / exposed	32 / 236 (13.56%)	20 / 146 (13.70%)	20 / 228 (8.77%)
occurrences (all)	44	23	26
Pain			
subjects affected / exposed	20 / 236 (8.47%)	13 / 146 (8.90%)	13 / 228 (5.70%)
occurrences (all)	22	14	15
Pyrexia			
subjects affected / exposed	54 / 236 (22.88%)	31 / 146 (21.23%)	34 / 228 (14.91%)
occurrences (all)	79	43	40
Temperature intolerance			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	7 / 236 (2.97%)	7 / 146 (4.79%)	14 / 228 (6.14%)
occurrences (all)	8	10	16
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 236 (0.42%)	2 / 146 (1.37%)	2 / 228 (0.88%)
occurrences (all)	1	2	3
Breast tenderness			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Vaginal mucosal blistering			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	63 / 236 (26.69%)	34 / 146 (23.29%)	30 / 228 (13.16%)
occurrences (all)	78	44	40
Dyspnoea			

subjects affected / exposed	36 / 236 (15.25%)	42 / 146 (28.77%)	35 / 228 (15.35%)
occurrences (all)	47	59	44
Dyspnoea exertional			
subjects affected / exposed	9 / 236 (3.81%)	6 / 146 (4.11%)	14 / 228 (6.14%)
occurrences (all)	9	6	14
Nasal congestion			
subjects affected / exposed	15 / 236 (6.36%)	12 / 146 (8.22%)	4 / 228 (1.75%)
occurrences (all)	17	13	4
Oropharyngeal pain			
subjects affected / exposed	12 / 236 (5.08%)	11 / 146 (7.53%)	10 / 228 (4.39%)
occurrences (all)	12	15	11
Pleural effusion			
subjects affected / exposed	5 / 236 (2.12%)	2 / 146 (1.37%)	11 / 228 (4.82%)
occurrences (all)	6	2	11
Pneumonitis			
subjects affected / exposed	3 / 236 (1.27%)	5 / 146 (3.42%)	2 / 228 (0.88%)
occurrences (all)	3	5	2
Productive cough			
subjects affected / exposed	9 / 236 (3.81%)	14 / 146 (9.59%)	5 / 228 (2.19%)
occurrences (all)	11	19	5
Pulmonary embolism			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	4 / 236 (1.69%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences (all)	5	1	1
Sinus congestion			
subjects affected / exposed	3 / 236 (1.27%)	2 / 146 (1.37%)	2 / 228 (0.88%)
occurrences (all)	3	3	2
Sinus disorder			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Upper airway cough syndrome			

subjects affected / exposed	7 / 236 (2.97%)	4 / 146 (2.74%)	4 / 228 (1.75%)
occurrences (all)	7	4	4
Wheezing			
subjects affected / exposed	7 / 236 (2.97%)	5 / 146 (3.42%)	1 / 228 (0.44%)
occurrences (all)	8	6	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	18 / 236 (7.63%)	12 / 146 (8.22%)	8 / 228 (3.51%)
occurrences (all)	19	12	9
Confusional state			
subjects affected / exposed	5 / 236 (2.12%)	4 / 146 (2.74%)	7 / 228 (3.07%)
occurrences (all)	5	4	7
Depression			
subjects affected / exposed	18 / 236 (7.63%)	11 / 146 (7.53%)	8 / 228 (3.51%)
occurrences (all)	19	12	8
Insomnia			
subjects affected / exposed	28 / 236 (11.86%)	21 / 146 (14.38%)	13 / 228 (5.70%)
occurrences (all)	30	21	14
Product issues			
Device occlusion			
subjects affected / exposed	0 / 236 (0.00%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 236 (6.36%)	10 / 146 (6.85%)	22 / 228 (9.65%)
occurrences (all)	20	13	28
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 236 (8.90%)	10 / 146 (6.85%)	23 / 228 (10.09%)
occurrences (all)	29	12	30
Bleeding time prolonged			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	15 / 236 (6.36%)	3 / 146 (2.05%)	19 / 228 (8.33%)
occurrences (all)	21	4	22
Blood creatinine increased			

subjects affected / exposed	22 / 236 (9.32%)	3 / 146 (2.05%)	8 / 228 (3.51%)
occurrences (all)	30	4	9
Body temperature increased			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	4 / 236 (1.69%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences (all)	7	1	2
Platelet count decreased			
subjects affected / exposed	3 / 236 (1.27%)	1 / 146 (0.68%)	3 / 228 (1.32%)
occurrences (all)	4	1	3
Weight decreased			
subjects affected / exposed	17 / 236 (7.20%)	15 / 146 (10.27%)	17 / 228 (7.46%)
occurrences (all)	20	19	21
Weight increased			
subjects affected / exposed	2 / 236 (0.85%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences (all)	2	4	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	2 / 228 (0.88%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	4 / 236 (1.69%)	8 / 146 (5.48%)	1 / 228 (0.44%)
occurrences (all)	5	12	1
Muscle strain			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences (all)	2	1	1
Splinter			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	1 / 236 (0.42%)	3 / 146 (2.05%)	3 / 228 (1.32%)
occurrences (all)	1	3	3
Tendon rupture			

subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences (all)	2	1	1
Palpitations			
subjects affected / exposed	3 / 236 (1.27%)	3 / 146 (2.05%)	0 / 228 (0.00%)
occurrences (all)	3	3	0
Sinus Tachycardia			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	3 / 228 (1.32%)
occurrences (all)	1	1	3
Tachycardia			
subjects affected / exposed	5 / 236 (2.12%)	2 / 146 (1.37%)	4 / 228 (1.75%)
occurrences (all)	5	2	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	24 / 236 (10.17%)	20 / 146 (13.70%)	20 / 228 (8.77%)
occurrences (all)	29	20	24
Dysgeusia			
subjects affected / exposed	9 / 236 (3.81%)	7 / 146 (4.79%)	3 / 228 (1.32%)
occurrences (all)	9	7	3
Headache			
subjects affected / exposed	36 / 236 (15.25%)	30 / 146 (20.55%)	32 / 228 (14.04%)
occurrences (all)	47	41	36
Hypoesthesia			
subjects affected / exposed	6 / 236 (2.54%)	5 / 146 (3.42%)	2 / 228 (0.88%)
occurrences (all)	6	6	3
Neuropathy peripheral			
subjects affected / exposed	14 / 236 (5.93%)	6 / 146 (4.11%)	9 / 228 (3.95%)
occurrences (all)	15	6	10
Paraesthesia			

subjects affected / exposed	6 / 236 (2.54%)	3 / 146 (2.05%)	4 / 228 (1.75%)
occurrences (all)	6	3	4
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences (all)	2	2	2
Sciatica			
subjects affected / exposed	0 / 236 (0.00%)	4 / 146 (2.74%)	2 / 228 (0.88%)
occurrences (all)	0	5	2
Tremor			
subjects affected / exposed	2 / 236 (0.85%)	3 / 146 (2.05%)	0 / 228 (0.00%)
occurrences (all)	2	3	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	58 / 236 (24.58%)	28 / 146 (19.18%)	42 / 228 (18.42%)
occurrences (all)	80	38	62
Anaemia Macrocytic			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 236 (0.42%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences (all)	1	3	1
Thrombocytopenia			
subjects affected / exposed	8 / 236 (3.39%)	2 / 146 (1.37%)	12 / 228 (5.26%)
occurrences (all)	16	2	14
Ear and labyrinth disorders			
Ear Congestion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Ear Discomfort			
subjects affected / exposed	5 / 236 (2.12%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences (all)	5	1	1
Ear Pain			
subjects affected / exposed	4 / 236 (1.69%)	2 / 146 (1.37%)	1 / 228 (0.44%)
occurrences (all)	4	2	1
Vertigo			

subjects affected / exposed	5 / 236 (2.12%)	2 / 146 (1.37%)	2 / 228 (0.88%)
occurrences (all)	5	2	2
Eye disorders			
Altered visual depth perception			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Eye Pruritus			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	2	1	0
Ulcerative keratitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	5 / 236 (2.12%)	7 / 146 (4.79%)	7 / 228 (3.07%)
occurrences (all)	5	7	7
Vitreous floaters			
subjects affected / exposed	1 / 236 (0.42%)	2 / 146 (1.37%)	0 / 228 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	33 / 236 (13.98%)	16 / 146 (10.96%)	13 / 228 (5.70%)
occurrences (all)	47	19	18
Abdominal pain upper			
subjects affected / exposed	11 / 236 (4.66%)	12 / 146 (8.22%)	7 / 228 (3.07%)
occurrences (all)	13	16	7
Constipation			
subjects affected / exposed	59 / 236 (25.00%)	35 / 146 (23.97%)	43 / 228 (18.86%)
occurrences (all)	81	39	52
Diarrhoea			

subjects affected / exposed	53 / 236 (22.46%)	31 / 146 (21.23%)	43 / 228 (18.86%)
occurrences (all)	92	63	56
Dry mouth			
subjects affected / exposed	9 / 236 (3.81%)	11 / 146 (7.53%)	8 / 228 (3.51%)
occurrences (all)	9	11	8
Dyspepsia			
subjects affected / exposed	6 / 236 (2.54%)	5 / 146 (3.42%)	5 / 228 (2.19%)
occurrences (all)	7	7	5
Dysphagia			
subjects affected / exposed	15 / 236 (6.36%)	8 / 146 (5.48%)	3 / 228 (1.32%)
occurrences (all)	18	8	3
Frequent bowl movements			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 236 (2.54%)	8 / 146 (5.48%)	7 / 228 (3.07%)
occurrences (all)	6	8	7
Haemorrhoids			
subjects affected / exposed	1 / 236 (0.42%)	6 / 146 (4.11%)	1 / 228 (0.44%)
occurrences (all)	1	6	1
Hypoaesthesia oral			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Loose tooth			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	63 / 236 (26.69%)	47 / 146 (32.19%)	63 / 228 (27.63%)
occurrences (all)	94	70	72
Oesophagitis			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	0 / 228 (0.00%)
occurrences (all)	0	2	0
Oral pain			
subjects affected / exposed	3 / 236 (1.27%)	2 / 146 (1.37%)	3 / 228 (1.32%)
occurrences (all)	3	2	4
Rectal haemorrhage			

subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	2 / 228 (0.88%)
occurrences (all)	2	1	2
Retching			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	0 / 228 (0.00%)
occurrences (all)	0	3	0
Stomatitis			
subjects affected / exposed	7 / 236 (2.97%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences (all)	7	3	1
Toothache			
subjects affected / exposed	2 / 236 (0.85%)	5 / 146 (3.42%)	1 / 228 (0.44%)
occurrences (all)	2	6	1
Vomiting			
subjects affected / exposed	44 / 236 (18.64%)	35 / 146 (23.97%)	45 / 228 (19.74%)
occurrences (all)	56	45	49
Salvary gland enlargement			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	3 / 236 (1.27%)	5 / 146 (3.42%)	2 / 228 (0.88%)
occurrences (all)	3	5	2
Dry skin			
subjects affected / exposed	25 / 236 (10.59%)	9 / 146 (6.16%)	6 / 228 (2.63%)
occurrences (all)	30	9	6
Erythema			
subjects affected / exposed	8 / 236 (3.39%)	5 / 146 (3.42%)	3 / 228 (1.32%)
occurrences (all)	11	5	3
Hyperhidrosis			
subjects affected / exposed	3 / 236 (1.27%)	5 / 146 (3.42%)	10 / 228 (4.39%)
occurrences (all)	3	6	11
Hyperkeratosis			
subjects affected / exposed	1 / 236 (0.42%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	1	1	0

Madarosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	13 / 236 (5.51%)	8 / 146 (5.48%)	7 / 228 (3.07%)
occurrences (all)	15	8	8
Pruritus			
subjects affected / exposed	41 / 236 (17.37%)	15 / 146 (10.27%)	28 / 228 (12.28%)
occurrences (all)	50	30	31
Pruritus generalised			
subjects affected / exposed	3 / 236 (1.27%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences (all)	3	0	1
Psoriasis			
subjects affected / exposed	3 / 236 (1.27%)	0 / 146 (0.00%)	1 / 228 (0.44%)
occurrences (all)	4	0	1
Rash			
subjects affected / exposed	35 / 236 (14.83%)	25 / 146 (17.12%)	18 / 228 (7.89%)
occurrences (all)	46	38	22
Rash maculo-papular			
subjects affected / exposed	10 / 236 (4.24%)	3 / 146 (2.05%)	2 / 228 (0.88%)
occurrences (all)	12	4	2
Rash pruritic			
subjects affected / exposed	2 / 236 (0.85%)	2 / 146 (1.37%)	1 / 228 (0.44%)
occurrences (all)	3	2	1
Rash vesicular			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Transient acantholytic dermatosis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Vitiligo			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	2	1	0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	12 / 236 (5.08%)	4 / 146 (2.74%)	3 / 228 (1.32%)
occurrences (all)	14	5	4
Nocturia			
subjects affected / exposed	4 / 236 (1.69%)	3 / 146 (2.05%)	1 / 228 (0.44%)
occurrences (all)	4	3	1
Pollakiuria			
subjects affected / exposed	9 / 236 (3.81%)	4 / 146 (2.74%)	1 / 228 (0.44%)
occurrences (all)	9	5	1
Proteinuria			
subjects affected / exposed	6 / 236 (2.54%)	2 / 146 (1.37%)	3 / 228 (1.32%)
occurrences (all)	11	2	5
Urethral obstruction			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	11 / 236 (4.66%)	6 / 146 (4.11%)	10 / 228 (4.39%)
occurrences (all)	12	6	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	44 / 236 (18.64%)	27 / 146 (18.49%)	21 / 228 (9.21%)
occurrences (all)	71	35	29
Arthritis			
subjects affected / exposed	3 / 236 (1.27%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	3	1	0
Back pain			
subjects affected / exposed	45 / 236 (19.07%)	29 / 146 (19.86%)	26 / 228 (11.40%)
occurrences (all)	53	38	29
Bone pain			
subjects affected / exposed	5 / 236 (2.12%)	4 / 146 (2.74%)	4 / 228 (1.75%)
occurrences (all)	6	4	5
Chrondrosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Flank pain			

subjects affected / exposed	10 / 236 (4.24%)	8 / 146 (5.48%)	4 / 228 (1.75%)
occurrences (all)	10	8	4
Joint swelling			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	3	1	0
Muscle spasms			
subjects affected / exposed	14 / 236 (5.93%)	7 / 146 (4.79%)	3 / 228 (1.32%)
occurrences (all)	17	8	3
Muscular weakness			
subjects affected / exposed	14 / 236 (5.93%)	7 / 146 (4.79%)	6 / 228 (2.63%)
occurrences (all)	17	9	7
Musculoskeletal chest pain			
subjects affected / exposed	7 / 236 (2.97%)	6 / 146 (4.11%)	11 / 228 (4.82%)
occurrences (all)	14	7	13
Musculoskeletal pain			
subjects affected / exposed	14 / 236 (5.93%)	19 / 146 (13.01%)	16 / 228 (7.02%)
occurrences (all)	15	23	18
Myalgia			
subjects affected / exposed	20 / 236 (8.47%)	11 / 146 (7.53%)	13 / 228 (5.70%)
occurrences (all)	24	12	13
Neck pain			
subjects affected / exposed	18 / 236 (7.63%)	9 / 146 (6.16%)	9 / 228 (3.95%)
occurrences (all)	19	10	10
Osteoarthritis			
subjects affected / exposed	2 / 236 (0.85%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	20 / 236 (8.47%)	13 / 146 (8.90%)	10 / 228 (4.39%)
occurrences (all)	26	21	12
Infections and infestations			
Bronchitis			
subjects affected / exposed	10 / 236 (4.24%)	2 / 146 (1.37%)	5 / 228 (2.19%)
occurrences (all)	13	2	7
Candida infection			
subjects affected / exposed	2 / 236 (0.85%)	3 / 146 (2.05%)	3 / 228 (1.32%)
occurrences (all)	2	3	3

Ear infection			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	2 / 236 (0.85%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	2	1	0
Herpes Zoster			
subjects affected / exposed	7 / 236 (2.97%)	1 / 146 (0.68%)	0 / 228 (0.00%)
occurrences (all)	7	1	0
Localised infection			
subjects affected / exposed	1 / 236 (0.42%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Lung infection			
subjects affected / exposed	0 / 236 (0.00%)	2 / 146 (1.37%)	1 / 228 (0.44%)
occurrences (all)	0	2	1
Nail bed infection			
subjects affected / exposed	0 / 236 (0.00%)	0 / 146 (0.00%)	0 / 228 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	12 / 236 (5.08%)	8 / 146 (5.48%)	4 / 228 (1.75%)
occurrences (all)	16	10	4
Pneumonia			
subjects affected / exposed	3 / 236 (1.27%)	6 / 146 (4.11%)	4 / 228 (1.75%)
occurrences (all)	4	6	4
Sinusitis			
subjects affected / exposed	9 / 236 (3.81%)	9 / 146 (6.16%)	1 / 228 (0.44%)
occurrences (all)	12	11	1
Tooth abscess			
subjects affected / exposed	5 / 236 (2.12%)	1 / 146 (0.68%)	1 / 228 (0.44%)
occurrences (all)	5	1	1
Upper respiratory tract infection			
subjects affected / exposed	27 / 236 (11.44%)	23 / 146 (15.75%)	14 / 228 (6.14%)
occurrences (all)	37	31	19
Urinary tract infection			
subjects affected / exposed	31 / 236 (13.14%)	13 / 146 (8.90%)	13 / 228 (5.70%)
occurrences (all)	42	20	15

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	69 / 236 (29.24%)	43 / 146 (29.45%)	54 / 228 (23.68%)
occurrences (all)	92	58	66
Dehydration			
subjects affected / exposed	16 / 236 (6.78%)	15 / 146 (10.27%)	13 / 228 (5.70%)
occurrences (all)	17	29	15
Hypercalcaemia			
subjects affected / exposed	12 / 236 (5.08%)	1 / 146 (0.68%)	4 / 228 (1.75%)
occurrences (all)	15	2	6
Hyperglycaemia			
subjects affected / exposed	8 / 236 (3.39%)	7 / 146 (4.79%)	6 / 228 (2.63%)
occurrences (all)	15	12	7
Hyperkalaemia			
subjects affected / exposed	9 / 236 (3.81%)	4 / 146 (2.74%)	14 / 228 (6.14%)
occurrences (all)	12	4	20
Hyperuricaemia			
subjects affected / exposed	0 / 236 (0.00%)	3 / 146 (2.05%)	0 / 228 (0.00%)
occurrences (all)	0	3	0
Hypokalaemia			
subjects affected / exposed	9 / 236 (3.81%)	4 / 146 (2.74%)	14 / 228 (6.14%)
occurrences (all)	12	4	20
Hypomagnesaemia			
subjects affected / exposed	11 / 236 (4.66%)	5 / 146 (3.42%)	12 / 228 (5.26%)
occurrences (all)	15	5	13
Hyponatraemia			
subjects affected / exposed	15 / 236 (6.36%)	6 / 146 (4.11%)	18 / 228 (7.89%)
occurrences (all)	16	8	21

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2012	Protocol was amended to include a broader patient population in expansion cohorts to better characterize the safety, tolerability, PD variability, and preliminary efficacy of single agent atezolizumab in different disease areas.
18 May 2012	Protocol was amended to include patients with other tumor types (e.g., head and neck cancer, esophageal cancer, gastric cancer, CRC, malignant lymphoma, or multiple myeloma) to further understand the indication-specific safety, immunogenicity, and pharmacodynamics of aPD-L1. Disease specific eligibility criteria, response assessments, and response criteria to evaluate anti-tumor activity in patients with malignant lymphoma or multiple myeloma were added. Exclusion criteria was modified to allow low risk patients with oligometastatic brain metastasis to participate in the trial, in order to understand the safety and antitumor activity of atezolizumab in patients with brain lesions. Eligibility criteria for a potential predictive biomarker dose expansion cohort (i.e., PD-L1 IHC selection criteria) was added, in order to identify patients who may derive more benefit from treatment with atezolizumab.
28 November 2012	Protocol was amended to include patients with other tumor types (e.g., pancreatic cancer, bladder cancer, sarcoma, acute myeloid leukemia, prostate, etc.) to further understand the indication-specific safety, immunogenicity, and pharmacodynamics of aPD-L1. Disease-specific eligibility criteria, response assessments, and response criteria to properly evaluate patients with acute myeloid leukemia (AML) were added. Up to 16 cycles of additional treatment for patients who remained in PR or CR at the end of initial treatment but who later relapsed within 2 years after the end of Cycle 16 was added. Clarification was added to the exclusion criteria regarding patients with risk of pulmonary toxicity; patients with pneumonitis (including drug-induced pneumonitis) or organizing pneumonia were added to the exclusion list, whereas patients with a history of radiation pneumonitis in the radiation field (fibrosis) were permitted. Revision of the exclusion criteria were made to exclude patients with secondary malignancy except for patients with non-melanoma skin cancer, carcinoma in situ of the cervix, or other malignancy from which the patient has been disease free for at least 5 years.
16 August 2013	Protocol was amended to update inclusion/exclusion criteria to exclude patients who may have been eligible for potentially curative therapies. Indication AML was removed; to better evaluate the safety of atezolizumab in patients with AML a separate first-in-human study was needed. Criteria for treatment with atezolizumab beyond progression was modified, to clearly define the minimal criteria that must be met by a patient with documented progressive disease. Dose and schedule of study treatment administered during the re-treatment stage as 15 mg/kg administered by IV infusion q3w was confirmed, regardless of which dose level the patients received during the initial treatment stage. Exclusion criteria was revised regarding autoimmune disease to allow patients with controlled Type 1 diabetes mellitus on a stable insulin regimen to enroll in the study.
30 April 2014	Protocol was amended with the addition of OS as an exploratory endpoint. Formulation and dosing of atezolizumab was updated with Phase III formulation and fixed dosing of 1200 mg. Treatment duration of atezolizumab was updated so that patients can receive atezolizumab treatment for as long as they continue to experience clinical benefit.

27 June 2014	Protocol was amended to include addition of patients with GBM, HCC, prostate cancer, and endometrial cancer to the tumor types for enrollment in the dose-expansion cohorts. Total number of patients for enrollment in the expansion cohort was updated from 295 patients to 495 patients; the total number of patients to be enrolled in the trial was revised from 456-489 patients to 656-689 patients. Mandatory tumor biopsy was added - if clinically feasible - at the first evidence of early radiographic disease progression, in order to characterize the kinetics and biological basis of the potential anti-tumor activity of atezolizumab. Inclusion criteria was revised to allow patients with certain autoimmune disease with dermatologic manifestations only, to be considered for enrollment if they meet the requirements specified in the protocol.
28 October 2015	Protocol was amended to include replacement of MPDL3280A (name of test product) with the approved international nonproprietary name, atezolizumab. Systemic immune activation (SIA) was identified as a potential risk of atezolizumab when given in combination with other immunomodulating agents. Management recommendations for early identification and management of SIA were included.
01 December 2016	Protocol was amended to include t1/2 of atezolizumab was updated to 27 days based upon clinical data, resulting in a change in the period during which female patients must remain abstinent or use contraception and the length of follow-up of pregnancy reporting from 90 days to 5 months after the last dose of atezolizumab and a change in the period during which patients must agree not to receive live, attenuated vaccine from 90 days to 5 months after the last dose of atezolizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported