Clinical trial results:
Open label multicenter Phase I/II study of the safety and efficacy of PDR001
administered to patients with advanced malignancies

Summary

EudraCT number	2014-003929-17
Trial protocol	DE NL FR ES HU NO IT
Global end of trial date	21 July 2020

Results information

Result version number	v1 (current)
This version publication date	06 August 2021
First version publication date	06 August 2021

Trial information

Trial identification

Sponsor protocol code	CPDR001X2101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02081378
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I :To estimate the recommended Phase II dose (RP2D) and/or the maximum tolerated dose (MTD) for spartalizumab

Phase ll: To estimate the anti-tumor activity of spartalizumab

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Lebanon: 3
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Norway: 11
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Spain: 55
Country: Number of subjects enrolled	Taiwan: 36
Country: Number of subjects enrolled	Thailand: 16
Country: Number of subjects enrolled	Turkey: 22
Country: Number of subjects enrolled	United States: 75

Worldwide total number of subjects	319
EEA total number of subjects	160

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)	202
From 65 to 84 years	114
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

58 patients were analyzed in Phase l and 261 patients were analyzed in Phase II of this study.

Pre-assignment

Screening details:

The study planned to analyze about 58 patients in Phase I and about 120 patients in Phase II.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	1 mg/kg q2w

Arm description:

Phase I Dose escalation cohort patients who took PDR001 1 mg/kg q2w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab was administered via iv infusion over 30 minutes (up to two hours, if clinically indicated) once every 2 weeks and the starting dose was 1 mg/kg

Arm title	3 mg/kg q2w

Arm description:

Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q2w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for infusion, Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab was administered via iv infusion over 30 minutes (up to two hours, if clinically indicated) once every 2 weeks and the starting dose was 1 mg/kg

Arm title	10mg/kg q2w

Arm description:

Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab was administered via iv infusion over 30 minutes (up to two hours, if clinically indicated) once every 2 weeks and the starting dose was 1 mg/kg

Arm title	3 mg/kg q4w

Arm description:

Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab was administered via iv infusion over 30 minutes (up to two hours, if clinically indicated) once every 2 weeks and the starting dose was 1 mg/kg

Arm title	5 mg/kg q4w

Arm description:

Phase I Dose escalation cohort patients who took PRD001 5 mg/kg q4w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab was administered via iv infusion over 30 minutes (up to two hours, if clinically indicated) once every 2 weeks and the starting dose was 1 mg/kg

Arm title	NSCLC 400mg/q4w

Arm description:

Phase II: non-small cell cancer patients who took PDR001 400 mg/q4w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were all treated with a flat dose of Spartalizumab 400 mg Q4W.

Arm title	Melanoma 400mg/q4w

Arm description:

Phase II: Melanoma patients who took PDR001 400 mg/q4w

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were all treated with a flat dose of Spartalizumab 400 mg Q4W.

Arm title	TNBC 400mg/q4w
Arm description:	
Phase II: Triple negative breast cancer (TNBC) patients who took PDR001 400 mg/q4w	
Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Subjects were all treated with a flat dose of Spartalizumab 400 mg Q4W.	
Arm title	NSCLC 300mg/q3w
Arm description:	
Phase II: non-small cell cancer patients who took PDR001 300 mg/q3w	
Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Subjects were all treated with a flat dose of Spartalizumab 300 mg Q3W.	
Arm title	ATC 400 mg/q4w
Arm description:	
Patients in Phase II with anaplastic thyroid cancer (ATC) who took PDR001 400 mg/q4w	
Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Subjects were all treated with a flat dose of Spartalizumab 400 mg Q4W.	

Number of subjects in period 1	1 mg/kg q2w	3 mg/kg q2w	10mg/kg q2w
Started	16	15	11
Completed	0	0	0
Not completed	16	15	11
Adverse event, serious fatal	1	1	1
Physician decision	-	1	-
Adverse event, non-fatal	1	-	-
Progressive Disease	14	11	7
Subject/Guardian Decision	-	2	3

Number of subjects in period 1	3 mg/kg q4w	5 mg/kg q4w	NSCLC 400mg/q4w

Started	6	10	59
Completed	0	0	0
Not completed	6	10	59
Adverse event, serious fatal	-	1	4
Physician decision	-	-	7
Adverse event, non-fatal	-	-	2
Progressive Disease	6	9	43
Subject/Guardian Decision	-	-	3

Number of subjects in period 1	Melanoma 400mg/q4w	TNBC 400mg/q4w	NSCLC 300mg/q3w
Started	61	40	59
Completed	0	0	0
Not completed	61	40	59
Adverse event, serious fatal	8	4	10
Physician decision	9	2	1
Adverse event, non-fatal	3	3	6
Progressive Disease	32	31	39
Subject/Guardian Decision	9	-	3

Number of subjects in period 1	ATC 400 mg/q4w
Started	42
Completed	0
Not completed	42
Adverse event, serious fatal	9
Physician decision	3
Adverse event, non-fatal	1
Progressive Disease	27
Subject/Guardian Decision	2

Baseline characteristics

Reporting groups	
Reporting group title	1 mg/kg q2w
Reporting group description:	
Phase I Dose escalation cohort patients who took PDR001 1 mg/kg q2w	
Reporting group title	3 mg/kg q2w
Reporting group description:	
Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q2w	
Reporting group title	10mg/kg q2w
Reporting group description:	
Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Reporting group title	3 mg/kg q4w
Reporting group description:	
Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Reporting group title	5 mg/kg q4w
Reporting group description:	
Phase I Dose escalation cohort patients who took PRD001 5 mg/kg q4w	
Reporting group title	NSCLC 400mg/q4w
Reporting group description:	
Phase II: non-small cell cancer patients who took PDR001 400 mg/q4w	
Reporting group title	Melanoma 400mg/q4w
Reporting group description:	
Phase II: Melanoma patients who took PDR001 400 mg/q4w	
Reporting group title	TNBC 400mg/q4w
Reporting group description:	
Phase II: Triple negative breast cancer (TNBC) patients who took PDR001 400 mg/q4w	
Reporting group title	NSCLC 300mg/q3w
Reporting group description:	
Phase II: non-small cell cancer patients who took PDR001 300 mg/q3w	
Reporting group title	ATC 400 mg/q4w
Reporting group description:	
Patients in Phase II with anaplastic thyroid cancer (ATC) who took PDR001 400 mg/q4w	

Reporting group values	1 mg/kg q2w	3 mg/kg q2w	10mg/kg q2w
Number of subjects	16	15	11
Age Categorical Units: Participants			
< 65 years	12	9	8
≥ 65years	4	6	3
Sex: Female, Male Units: Participants			
Female	9	7	4
Male	7	8	7
Race/Ethnicity, Customized Units: Subjects			
Caucasian	10	14	8
Black	2	0	0
Asian	3	1	2

Unknown	1	0	0
Other	0	0	1

Reporting group values	3 mg/kg q4w	5 mg/kg q4w	NSCLC 400mg/q4w
Number of subjects	6	10	59
Age Categorical Units: Participants			
< 65 years	6	8	33
≥ 65years	0	2	26
Sex: Female, Male Units: Participants			
Female	2	4	23
Male	4	6	36
Race/Ethnicity, Customized Units: Subjects			
Caucasian	4	8	42
Black	0	0	0
Asian	2	1	12
Unknown	0	0	5
Other	0	1	0

Reporting group values	Melanoma 400mg/q4w	TNBC 400mg/q4w	NSCLC 300mg/q3w
Number of subjects	61	40	59
Age Categorical Units: Participants			
< 65 years	37	29	35
≥ 65years	24	11	24
Sex: Female, Male Units: Participants			
Female	22	40	20
Male	39	0	39
Race/Ethnicity, Customized Units: Subjects			
Caucasian	37	32	50
Black	1	1	0
Asian	23	4	8
Unknown	0	2	1
Other	0	1	0

Reporting group values	ATC 400 mg/q4w	Total	
Number of subjects	42	319	
Age Categorical Units: Participants			
< 65 years	25	202	
≥ 65years	17	117	
Sex: Female, Male Units: Participants			
Female	19	150	
Male	23	169	

Race/Ethnicity, Customized Units: Subjects			
Caucasian	33	238	
Black	1	5	
Asian	4	60	
Unknown	4	13	
Other	0	3	

Subject analysis sets

Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Full analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PDR001 10 mg/kg q2w	
Subject analysis set title	3mg/kg q4w
Subject analysis set type	Full analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	3mg/kg q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Full analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Full analysis
Subject analysis set description: Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Full analysis
Subject analysis set description: Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	TNBC 400 mg/q4w
Subject analysis set type	Full analysis
Subject analysis set description: Patients in Phase II with TNBC who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Full analysis
Subject analysis set description: Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	NSCLC 400 mg/q4w

Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	TNBC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with TNBC who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	3mg/kg q4w
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	Phase 1 Part
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Combination of all the patients who were enrolled in the phase one part of the study. All the patients received varying doses of the study drug, PDR001.	

Subject analysis set title	Phase 2 Part
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combination of all the patients who were enrolled in the phase II part of the study. All the patients received varying doses of the study drug, PDR001.

Reporting group values	10 mg/kg q2w	3mg/kg q4w	10 mg/kg q2w
Number of subjects	11	6	4
Age Categorical Units: Participants			
< 65 years	8	6	
≥ 65years	3	0	
Sex: Female, Male Units: Participants			
Female	4	2	
Male	7	4	
Race/Ethnicity, Customized Units: Subjects			
Caucasian	8	4	
Black	0	0	
Asian	2	2	
Unknown	0	0	
Other	1	0	

Reporting group values	3mg/kg q4w	10 mg/kg q2w	NSCLC 400 mg/q4w
Number of subjects	3	11	59
Age Categorical Units: Participants			
< 65 years			
≥ 65years			
Sex: Female, Male Units: Participants			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			
Black			
Asian			
Unknown			
Other			

Reporting group values	Melanoma 400 mg/q4w	TNBC 400 mg/q4w	NSCLC 300 mg/q3w
Number of subjects	61	40	59
Age Categorical Units: Participants			
< 65 years			
≥ 65years			
Sex: Female, Male Units: Participants			
Female			

Male			

Race/Ethnicity, Customized Units: Subjects			
Caucasian Black Asian Unknown Other			

Reporting group values	10 mg/kg q2w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w
Number of subjects	3	52	54
Age Categorical Units: Participants			
< 65 years ≥ 65years			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian Black Asian Unknown Other			

Reporting group values	TNBC 400 mg/q4w	NSCLC 300 mg/q3w	10 mg/kg q2w
Number of subjects	33	46	6
Age Categorical Units: Participants			
< 65 years ≥ 65years			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian Black Asian Unknown Other			

Reporting group values	3mg/kg q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w
Number of subjects	6	9	17

Age Categorical Units: Participants			
< 65 years ≥ 65years			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian Black Asian Unknown Other			

Reporting group values	NSCLC 300 mg/q3w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w
Number of subjects	4	11	19
Age Categorical Units: Participants			
< 65 years ≥ 65years			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian Black Asian Unknown Other			

Reporting group values	NSCLC 300 mg/q3w	Phase 1 Part	Phase 2 Part
Number of subjects	5	58	261
Age Categorical Units: Participants			
< 65 years ≥ 65years			
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Caucasian Black Asian Unknown Other			

End points

End points reporting groups

Reporting group title	1 mg/kg q2w
Reporting group description: Phase I Dose escalation cohort patients who took PDR001 1 mg/kg q2w	
Reporting group title	3 mg/kg q2w
Reporting group description: Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q2w	
Reporting group title	10mg/kg q2w
Reporting group description: Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Reporting group title	3 mg/kg q4w
Reporting group description: Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Reporting group title	5 mg/kg q4w
Reporting group description: Phase I Dose escalation cohort patients who took PRD001 5 mg/kg q4w	
Reporting group title	NSCLC 400mg/q4w
Reporting group description: Phase II: non-small cell cancer patients who took PDR001 400 mg/q4w	
Reporting group title	Melanoma 400mg/q4w
Reporting group description: Phase II: Melanoma patients who took PDR001 400 mg/q4w	
Reporting group title	TNBC 400mg/q4w
Reporting group description: Phase II: Triple negative breast cancer (TNBC) patients who took PDR001 400 mg/q4w	
Reporting group title	NSCLC 300mg/q3w
Reporting group description: Phase II: non-small cell cancer patients who took PDR001 300 mg/q3w	
Reporting group title	ATC 400 mg/q4w
Reporting group description: Patients in Phase II with anaplastic thyroid cancer (ATC) who took PDR001 400 mg/q4w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Full analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PDR001 10 mg/kg q2w	
Subject analysis set title	3mg/kg q4w
Subject analysis set type	Full analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	3mg/kg q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description: Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Subject analysis set title	10 mg/kg q2w

Subject analysis set type	Full analysis
Subject analysis set description:	
Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	TNBC 400 mg/q4w
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients in Phase II with TNBC who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	TNBC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with TNBC who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	10 mg/kg q2w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w	
Subject analysis set title	3mg/kg q4w
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w

Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	NSCLC 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 400 mg/q4w	
Subject analysis set title	Melanoma 400 mg/q4w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with Melanoma who took PDR001 400 mg/q4w	
Subject analysis set title	NSCLC 300 mg/q3w
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in Phase II with non-small cell cancer who took PDR001 300 mg/q3w	
Subject analysis set title	Phase 1 Part
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Combination of all the patients who were enrolled in the phase one part of the study. All the patients received varying doses of the study drug, PDR001.	
Subject analysis set title	Phase 2 Part
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Combination of all the patients who were enrolled in the phase II part of the study. All the patients received varying doses of the study drug, PDR001.	

Primary: Phase I: The exposure (AUC(0-336h)) after first dose of treatment at cycle 3 (each cycle = 28 days)

End point title	Phase I: The exposure (AUC(0-336h)) after first dose of treatment at cycle 3 (each cycle = 28 days)[1][2]
End point description:	
Estimated the recommended phase 2 dose (RP2D) and/or the maximum tolerated dose (MTD) for PDR001. AUC0-336h is the AUC from time zero to 336 hour post dose of a measurable concentration sampling time.	
End point type	Primary
End point timeframe:	
Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (cycle 3)	

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 analysis planned

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	8	4	4	4
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	270 (± 52.5)	1150 (± 51.1)	1490 (± 34.2)	3110 (± 33.1)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	575 (± 21.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Phase I: Incidence of dose limiting toxicities (DLTs)

End point title	Phase I: Incidence of dose limiting toxicities (DLTs)[3][4]

End point description:

DLT is defined as an adverse event (AE) or abnormal laboratory value of common terminology criteria for adverse events (CTCAE) grade ≥ 3 assessed as unrelated to disease, disease progression, inter-current illness or concomitant medications, which occurs within the first cycle of treatment with PDR001 during the dose escalation part of the study for which relationship to study treatment cannot be ruled out, with some exceptions.

End point type	Primary

End point timeframe:

8 months

Notes:

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

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	11
Units: Participants	0	0	0	0

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			

Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Phase ll: Overall response Rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST v1.1)

End point title	Phase ll: Overall response Rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST v1.1)[5][6]

End point description:

ORR is the percentage of participants with a best overall response of complete response (CR) or partial response (PR) as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
CR = at least 2 determinations of CR at least 4 weeks apart before progression where confirmation required or 1 determination of CR prior to progression where confirmation not required.
PR = at least 2 determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or 1 determination of PR prior to progression where confirmation not required.
RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Primary

End point timeframe:

61 months

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 analysis planned

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: Percentage of participants				
number (confidence interval 90%)	19.0 (9.8 to 31.8)	15.3 (8.2 to 25.1)	27.9 (18.6 to 38.8)	0.0 (0.0 to 7.2)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Percentage of participants				
number (confidence interval 90%)	6.8 (2.3 to 14.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Serum pharmacokinetic (PK) parameter AUCs (AUC0-336h (cycle 1 only), AUCinf, AUClast AUCtau)

End point title	Phase I: Serum pharmacokinetic (PK) parameter AUCs (AUC0-336h (cycle 1 only), AUCinf, AUClast AUCtau)[7]

End point description:

AUC0-336h is the AUC from time zero to 336 hour post dose of a measurable concentration sampling time.
AUClast: The AUC from time zero to the last measurable concentration sampling time (tlast) (mass x time x volume-1).
AUCinf: The AUC from time zero to infinity (mass x time x volume-1).
AUCtau: The AUC calculated to the end of a dosing interval (tau) at steady-state (amount x time x volume-1).

End point type	Secondary

End point timeframe:

Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (cycle 1 & 3)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	11
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle (C) 1: AUC0-336h (n=16, 13, 10, 6, 10)	126 (± 29.5)	324 (± 24.4)	638 (± 35.3)	1270 (± 20.3)
C1: AUCinf (n = 1, 0,0,2,3)	123 (± 0)	999 (± 999)	726 (± 16.0)	999 (± 999)
C1: AUClast	125 (± 29.9)	353 (± 31.4)	943 (± 37.4)	1240 (± 21.6)
C1: AUCtau (n = 16, 13, 10, 6, 10)	126 (± 29.5)	324 (± 24.4)	984 (± 41.9)	1270 (± 20.3)
C3: AUClast	260 (± 44.8)	995 (± 60.5)	2560 (± 37.2)	2520 (± 58.4)
C3: AUCtau (n = 8, 4, 4, 2, 2)	270 (± 52.5)	1150 (± 51.1)	2770 (± 26.6)	3110 (± 33.1)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle (C) 1: AUC0-336h (n=16, 13, 10, 6, 10)	350 (± 35.0)			
C1: AUCinf (n = 1, 0,0,2,3)	384 (± 9.8)			
C1: AUClast	522 (± 39.1)			
C1: AUCtau (n = 16, 13, 10, 6, 10)	524 (± 39.6)			
C3: AUClast	933 (± 21.3)			
C3: AUCtau (n = 8, 4, 4, 2, 2)	1040 (± 19.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Serum pharmacokinetic (PK) parameter Cmax

End point title	Phase I: Serum pharmacokinetic (PK) parameter Cmax[8]

End point description:

The maximum (peak) observed plasma, blood, serum, or other body fluid drug concentration after single dose administration (mass x volume-1)

End point type	Secondary

End point timeframe:

Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (Cycle 1 & 3)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	11
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
C1 (n = 15, 15, 10, 6, 9)	18.2 (± 26.5)	53.8 (± 23.6)	106 (± 34.2)	185 (± 18.3)
C3 (n = 10, 7, 3, 3, 2)	29.7 (± 41.0)	112 (± 27.3)	179 (± 45.2)	312 (± 30.0)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
C1 (n = 15, 15, 10, 6, 9)	53.8 (± 29.4)			
C3 (n = 10, 7, 3, 3, 2)	69.7 (± 9.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Serum pharmacokinetic (PK) parameter Tmax

End point title	Phase I: Serum pharmacokinetic (PK) parameter Tmax[9]

End point description:

The time to reach maximum (peak) plasma, blood, serum, or other body fluid drug concentration after single dose administration (time)

End point type	Secondary

End point timeframe:

Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (cycle 1 & 3)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	11
Units: hour				
median (full range (min-max))				
C1 (n = 15, 15, 10, 6, 9)	1.58 (1.38 to 2.12)	1.57 (1.25 to 1.7)	1.58 (1.08 to 1.67)	1.55 (1.13 to 1.68)
C3 (n = 10, 7, 3, 3, 2)	1.55 (1.45 to 1.75)	1.55 (0.75 to 1.58)	1.3 (0.783 to 1.82)	1.58 (1.52 to 1.62)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: hour				
median (full range (min-max))				
C1 (n = 15, 15, 10, 6, 9)	1.55 (1.5 to 1.83)			
C3 (n = 10, 7, 3, 3, 2)	1.5 (1.5 to 1.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Serum pharmacokinetic (PK) parameter AUCs (AUC336h, AUCinf, AUClast, AUCtau)

End point title	Phase II: Serum pharmacokinetic (PK) parameter AUCs (AUC336h, AUCinf, AUClast, AUCtau)[10]

End point description:

AUC0-336h is the AUC from time zero to 336 hour post dose of a measurable concentration sampling time.
AUClast: The AUC from time zero to the last measurable concentration sampling time (tlast) (mass x time x volume-1).
AUCinf: The AUC from time zero to infinity (mass x time x volume-1).
AUCtau: The AUC calculated to the end of a dosing interval (tau) at steady-state (amount x time x volume-1).

End point type	Secondary

End point timeframe:

Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (cycle 1 & 3)

Notes:

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

Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
C1: AUC0-336h (n =58, 58, 37, 54, 37)	704 (± 28.2)	681 (± 39.4)	775 (± 31.7)	752 (± 29.3)
C1: AUCinf (n = 13, 8, 7, 5, 2)	1160 (± 7.1)	1090 (± 29.6)	1080 (± 45.4)	1240 (± 25.2)
C1: AUClast	865 (± 69.8)	980 (± 42.5)	1020 (± 109.9)	923 (± 76.1)
C1: AUCtau (n= 54, 55, 32, 48, 36)	1070 (± 31.3)	1010 (± 39.8)	1190 (± 35.0)	1130 (± 34.9)
C3: AUC0-336h (n = 36, 49, 12, 40, 16)	1290 (± 30.0)	1210 (± 36.3)	1140 (± 43.8)	1360 (± 45.7)
C3: AUCinf (n = 1, 1, 1, 1, 0)	999 (± 999)	1050 (± 999)	1070 (± 999)	2340 (± 999)
C3: AUClast (n = 37, 51, 16, 44, 19)	1600 (± 88.0)	1860 (± 39.9)	1650 (± 59.7)	1630 (± 73.4)
C3: AUCtau (n= 31, 44, 7, 38, 14)	2120 (± 32.7)	1940 (± 35.5)	1790 (± 53.4)	1920 (± 44.4)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
C1: AUC0-336h (n =58, 58, 37, 54, 37)	535 (± 29.3)			
C1: AUCinf (n = 13, 8, 7, 5, 2)	491 (± 22.7)			
C1: AUClast	602 (± 62.2)			
C1: AUCtau (n= 54, 55, 32, 48, 36)	689 (± 40.4)			
C3: AUC0-336h (n = 36, 49, 12, 40, 16)	850 (± 50.6)			
C3: AUCinf (n = 1, 1, 1, 1, 0)	135 (± 999)			
C3: AUClast (n = 37, 51, 16, 44, 19)	984 (± 78.0)			
C3: AUCtau (n= 31, 44, 7, 38, 14)	1100 (± 54.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Serum pharmacokinetic (PK) parameter Cmax

End point title	Phase II: Serum pharmacokinetic (PK) parameter Cmax[11]

End point description:

The maximum (peak) observed plasma, blood, serum, or other body fluid drug concentration after single dose administration (mass x volume-1)

End point type	Secondary

End point timeframe:

Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (Cycle 1 & 3)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
C1 (n = 52, 58, 32, 55, 35)	100 (± 27.3)	103 (± 37.0)	111 (± 26.6)	114 (± 23.6)
C3 (n = 33, 45, 11, 39, 18)	146 (± 22.6)	151 (± 32.0)	141 (± 33.4)	163 (± 34.7)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
C1 (n = 52, 58, 32, 55, 35)	79.9 (± 31.8)			
C3 (n = 33, 45, 11, 39, 18)	103 (± 36.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Serum pharmacokinetic (PK) parameter Tmax

End point title	Phase II: Serum pharmacokinetic (PK) parameter Tmax[12]

End point description:

The time to reach maximum (peak) plasma, blood, serum, or other body fluid drug concentration after single dose administration (time)

End point type	Secondary

End point timeframe:

Predose, 1hour (h), 24h, 48h, 72h, 168h, 240h, 336h post dose (Cycle 1 & 3)

Notes:

[12] - 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 analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: hour				
median (full range (min-max))				
C1 (n= 52, 58, 32, 55, 35)	1.55 (0.5 to 2.75)	1.58 (0.55 to 2.52)	1.58 (1.07 to 2.9)	1.58 (1.18 to 2.15)
C3 (n = 33, 45, 11, 39, 18)	1.57 (0 to 4.63)	1.6 (0.983 to 2.08)	1.55 (1.07 to 2.22)	1.53 (1.42 to 1.62)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: hour				
median (full range (min-max))				
C1 (n= 52, 58, 32, 55, 35)	1.65 (1.00 to 3.08)			
C3 (n = 33, 45, 11, 39, 18)	1.58 (1.33 to 2.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Presence and/or concentration of anti-PDR001

End point title	Phase I: Presence and/or concentration of anti-PDR001[13]

End point description:

Assessed PDR001 anti-drug anti-body (ADA) incidence in Phase I patients - the emergence of anti-PDR001 antibodies following one or more intravenous (i.v.) infusions of PDR001. Each cycle = 28 days; End of treatment was expected to be on average 1 year after the start of study treatment.
For Treatment-induced ADA-positive, percentage was based on patients ADA-negative at baseline.
For Treatment-boosted ADA-positive, percentage was based on patients ADA-positive at baseline.

End point type	Secondary

End point timeframe:

42 months

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	11	10	3
Units: Participants				
Patients with ADA-negative sample at baseline	11	9	9	1
Patients with ADA-positive sample at baseline	5	2	1	2

ADA-negative	10	8	8	1
ADA-positive (i.e., ADA incidence)	4	2	1	2
Treatment-induced ADA-positive	1	1	1	0
Treatment-boosted ADA-positive	3	1	0	2

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: Participants				
Patients with ADA-negative sample at baseline	5			
Patients with ADA-positive sample at baseline	1			
ADA-negative	4			
ADA-positive (i.e., ADA incidence)	1			
Treatment-induced ADA-positive	1			
Treatment-boosted ADA-positive	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Presence and/or concentration of anti-PDR001

End point title	Phase II: Presence and/or concentration of anti-PDR001[14]

End point description:

Assessed PDR001 anti-drug anti-body (ADA) incidence in Phase I patients - the emergence of anti-PDR001 antibodies following one or more intravenous (i.v.) infusions of PDR001. Each cycle = 28 days; End of treatment was expected to be on average 1 year after the start of study treatment.
For Treatment -induced ADA-positive, Percentage was based on subjects ADA-negative at baseline.
For Treatment-boosted ADA-positive, Percentage was based on subjects ADA-positive at baseline.

End point type	Secondary

End point timeframe:

42 months

Notes:

[14] - 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 analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	52	54	33
Units: Participants				
Patients with ADA-negative sample at baseline	29	43	48	29
Patients with ADA-positive sample at baseline	2	9	6	4
ADA-negative	24	34	46	23
ADA-positive (i.e., ADA incidence)	6	11	4	7

Treatment-induced ADA-positive	5	9	2	6
Treatment-boosted ADA-positive	1	2	2	1

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: Participants				
Patients with ADA-negative sample at baseline	41			
Patients with ADA-positive sample at baseline	5			
ADA-negative	31			
ADA-positive (i.e., ADA incidence)	12			
Treatment-induced ADA-positive	10			
Treatment-boosted ADA-positive	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Overall Response Rate (ORR) as per Investigator based on RECIST v1.1

End point title	Phase I: Overall Response Rate (ORR) as per Investigator based on RECIST v1.1[15]

End point description:

ORR is the percentage of participants with a best overall response of complete response CR or partial response PR as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required.
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Secondary

End point timeframe:

27 months

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	11
Units: Percentage of participants				
number (confidence interval 90%)	0.00 (0.0 to 17.1)	6.7 (0.3 to 27.9)	0.0 (0.0 to 25.9)	9.1 (0.5 to 36.4)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: Percentage of participants				
number (confidence interval 90%)	0.0 (0.0 to 39.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Disease Control Rate (DCR) as per Investigator based on RECIST v1.1

End point title	Phase I: Disease Control Rate (DCR) as per Investigator based on RECIST v1.1[16]

End point description:

DCR is the percentage of patients with a best overall response of CR or PR or stable disease (SD).
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
SD = at least one SD assessment (or better) > 6 weeks after randomization/start of treatment (and not qualifying for CR or PR).
RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Secondary

End point timeframe:

27 months

Notes:

[16] - 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 analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	3 mg/kg q4w	5 mg/kg q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	6	10
Units: Percentage of participants				
number (confidence interval 90%)	56.3 (33.3 to 77.3)	46.7 (24.4 to 70.0)	50.0 (15.3 to 84.7)	20.0 (3.7 to 50.7)

End point values	10 mg/kg q2w			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: Percentage of participants				

number (confidence interval 90%)	27.3 (7.9 to 56.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Progression Free Survival (PFS) as per RECIST v1.1

End point title	Phase I: Progression Free Survival (PFS) as per RECIST v1.1[17]

End point description:

PFS is the time from date of start of treatment to the date of event defined as the first documented progression or death due to any cause. PFS is per Kaplan-Meier estimates.
RECIST criteria, published in February 2000 by an international collaboration including the European Organization for Research and Treatment of Cancer (EORTC), National Cancer Institute of the United States, and the National Cancer Institute of Canada Clinical Trials Group, is a Response evaluation criteria in solid tumors is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.
RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Secondary

End point timeframe:

27 months

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	6
Units: Percentage of participants				
median (confidence interval 90%)	3.5 (1.8 to 6.5)	1.9 (1.5 to 8.1)	1.8 (1.1 to 1.8)	2.2 (1.7 to 5.8)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: Percentage of participants				
median (confidence interval 90%)	2.7 (1.1 to 3.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Duration of Response (DOR) as per RECIST v1.1

End point title	Phase I: Duration of Response (DOR) as per RECIST v1.1[18]

End point description:

DOR: measured from the time measurement criteria are met for CR or PR (whichever status is recorded first) until the first date that recurrence or PD is objectively documented. CR = at least 2 determinations of CR at least 4 weeks apart before progression where confirmation required or 1 determination of CR prior to progression where confirmation not required; PR = at least 2 determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or 1 determination of PR prior to progression where confirmation not required; PD =progression <= 12 weeks after randomization/start of treatment (and not qualifying for CR, PR or SD). SD = at least 1 SD assessment (or better) > 6 weeks after randomization/start of treatment (and not qualifying for CR or PR). RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment

End point type	Secondary

End point timeframe:

61 months

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	3 mg/kg q2w	10mg/kg q2w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: months				
arithmetic mean (full range (min-max))	261.00 (261.0 to 261.0)	55.00 (55.0 to 55.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase l only: Overall Response Rate (ORR) as per Investigator based on immune related response criteria (irRC)

End point title	Phase l only: Overall Response Rate (ORR) as per Investigator based on immune related response criteria (irRC)[19]

End point description:

ORR is the percentage of participants with a best overall response of complete response (CR) or partial response (PR) as per irRC.
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required.
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
The immune-related response criteria (irRC) is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug.

End point type	Secondary

End point timeframe:

27 months

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	10mg/kg q2w	5 mg/kg q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	11	10
Units: Percentage of participants				
number (confidence interval 90%)	0.00 (0.0 to 17.1)	6.7 (0.3 to 27.9)	9.1 (0.5 to 36.4)	0.0 (0.0 to 25.9)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: Percentage of participants				
number (confidence interval 90%)	0.0 (0.0 to 39.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase l only: Disease Control Rate (DCR) as per Investigator based on irRC

End point title	Phase l only: Disease Control Rate (DCR) as per Investigator based on irRC[20]

End point description:

DCR is the percentage of patients with a best overall response of CR or PR or stable disease (SD).
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
SD = at least one SD assessment (or better) > 6 weeks after randomization/start of treatment (and not qualifying for CR or PR).
The immune-related response criteria (irRC) is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug.

End point type	Secondary

End point timeframe:

27 months

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	10mg/kg q2w	3 mg/kg q4w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	11	6
Units: Percentage of participants				
number (confidence interval 90%)	62.5 (39.1 to 82.2)	53.3 (30.0 to 75.6)	27.3 (7.9 to 56.4)	50.0 (15.3 to 84.7)

End point values	5 mg/kg q4w			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage of participants				
number (confidence interval 90%)	30.0 (8.7 to 60.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase l only: Progression Free Survival (PFS) as per irRC

End point title	Phase l only: Progression Free Survival (PFS) as per irRC[21]

End point description:

PFS is the time from date of start of treatment to the date of event defined as the first documented progression or death due to any cause. PFS is per Kaplan-Meier estimates.
The immune-related response criteria (irRC) is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug.

End point type	Secondary

End point timeframe:

27 months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	1 mg/kg q2w	3 mg/kg q2w	5 mg/kg q4w	10 mg/kg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16	15	10	11
Units: Percentage of participants				
median (confidence interval 90%)	3.6 (1.8 to 999)	2.7 (1.5 to 8.1)	1.8 (1.1 to 2.8)	2.2 (1.7 to 5.8)

End point values	3mg/kg q4w			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: Percentage of participants				
median (confidence interval 90%)	2.7 (1.1 to 5.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase I: Duration of Response (DOR) as per irRC

End point title	Phase I: Duration of Response (DOR) as per irRC[22]

End point description:

DOR: measured from time measurement criteria are met for CR or PR (whichever status is recorded first) until first date that recurrence or PD is objectively documented
CR: at least 2 determinations of CR at least 4 weeks apart before progression where confirmation required or 1 determination of CR prior to progression where confirmation not required
PR: at least 1 determination of PR or better at least 4 weeks apart before progression (& not qualifying for a CR) where confirmation required or 1 determination of PR prior to progression where confirmation not required
PD: progression <= start of treatment (& not qualifying for CR, PR or SD)
SD: at least 1 SD assessment (or better) > 6 weeks after randomization/start of treatment (& not qualifying for CR or PR)
irRC is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug

End point type	Secondary

End point timeframe:

61 months

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	3 mg/kg q2w	10mg/kg q2w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: months				
arithmetic mean (full range (min-max))	261.00 (261.0 to 261.0)	55.00 (55.0 to 55.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Disease control rate (DCR) as per Investigator based on RECIST v1.1

End point title	Phase II: Disease control rate (DCR) as per Investigator based on RECIST v1.1[23]

End point description:

DCR is the percentage of patients with a best overall response of CR or PR or stable disease (SD).
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
SD = at least one SD assessment (or better) > 6 weeks after randomization/start of treatment (and not qualifying for CR or PR).
RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Secondary

End point timeframe:

61 months

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: Percentage of participants				
number (confidence interval 90%)	31.0 (19.4 to 44.6)	49.2 (37.8 to 60.5)	62.3 (51.0 to 72.7)	20.0 (10.4 to 33.2)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Percentage of participants				
number (confidence interval 90%)	35.6 (25.2 to 47.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Progression Free Survival as per Investigator based on RECIST v1.1

End point title	Phase II: Progression Free Survival as per Investigator based on RECIST v1.1[24]

End point description:

PFS is the time from date of start of treatment to the date of event defined as the first documented progression or death due to any cause. PFS is per Kaplan-Meier estimates.
RECIST criteria, published in February 2000 by an international collaboration including the European Organization for Research and Treatment of Cancer (EORTC), National Cancer Institute of the United States, and the National Cancer Institute of Canada Clinical Trials Group, is a Response evaluation criteria in solid tumors is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Secondary

End point timeframe:

61 months

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: Percentage of participants				
median (confidence interval 90%)	1.7 (1.4 to 1.9)	2.7 (1.9 to 5.4)	4.7 (3.5 to 5.6)	1.7 (1.7 to 1.8)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Percentage of participants				
median (confidence interval 90%)	1.9 (1.8 to 2.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Duration of response (DOR) as per Investigator based on RECIST v1.1

End point title	Phase II: Duration of response (DOR) as per Investigator based on RECIST v1.1[25]

End point description:

DOR is measured from the time measurement criteria are met for CR or PR (whichever status is recorded first) until the first date that recurrence or PD is objectively documented.
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
PD = progression <= start of treatment (and not qualifying for CR, PR or SD).
SD = at least one SD assessment (or better) > 6 weeks after randomization/start of treatment (and not qualifying for CR or PR).
RECIST criteria is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment.

End point type	Secondary

End point timeframe:

61 months

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	NSCLC 300 mg/q3w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	9	17	4
Units: months				
median (confidence interval 90%)	22.8 (5.7 to 999)	5.6 (3.9 to 16.6)	32.0 (11.1 to 999)	10.9 (3.7 to 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Overall response rate (ORR) as per Investigator based on irRC

End point title	Phase II: Overall response rate (ORR) as per Investigator based on irRC[26]

End point description:

ORR is the percentage of participants with a best overall response CR or PR as per irRC.
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required.
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
The immune-related response criteria (irRC) is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug.

End point type	Secondary

End point timeframe:

61 months

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: Percentage of participants				
number (confidence interval 90%)	23.8 (13.5 to 37.0)	18.6 (10.8 to 29.0)	31.1 (21.5 to 42.3)	0.0 (0.0 to 7.2)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Percentage of participants				
number (confidence interval 90%)	8.5 (3.4 to 17.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Disease Control rate (DCR) as per Investigator based on irRC

End point title	Phase II: Disease Control rate (DCR) as per Investigator based on irRC[27]

End point description:

DCR is the percentage of patients with a best overall response of CR or PR or stable disease (SD).
CR = at least two determinations of CR at least 4 weeks apart before progression where confirmation required or one determination of CR prior to progression where confirmation not required
PR = at least two determinations of PR or better at least 4 weeks apart before progression (and not qualifying for a CR) where confirmation required or one determination of PR prior to progression where confirmation not required.
SD = at least one SD assessment (or better) > 6 weeks after randomization/start of treatment (and not qualifying for CR or PR).
The immune-related response criteria (irRC) is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug.

End point type	Secondary

End point timeframe:

61 months

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: Percentage of participants				
number (confidence interval 90%)	35.7 (23.5 to 49.5)	55.9 (44.4 to 67.0)	67.2 (56.0 to 77.1)	22.5 (12.3 to 36.0)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Percentage of participants				
number (confidence interval 90%)	39.0 (28.3 to 50.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Progression Free Survival (PFS) per irRC

End point title	Phase II: Progression Free Survival (PFS) per irRC[28]

End point description:

PFS is the time from date of start of treatment to the date of event defined as the first documented progression or death due to any cause. PFS is per Kaplan-Meier estimates.
The immune-related response criteria (irRC) is a set of published rules that define when tumors in

cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug.

End point type	Secondary

End point timeframe:

61 months

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	TNBC 400 mg/q4w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	59	61	40
Units: Percentage of participants				
median (confidence interval 90%)	1.7 (1.4 to 1.9)	3.7 (2.6 to 7.1)	5.4 (3.7 to 6.5)	1.8 (1.7 to 1.8)

End point values	NSCLC 300 mg/q3w			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Percentage of participants				
median (confidence interval 90%)	2.0 (1.8 to 2.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase II: Duration of response (DOR) per irRC

End point title	Phase II: Duration of response (DOR) per irRC[29]

End point description:

DOR: measured from time measurement criteria are met for CR or PR (whichever status is recorded first) until first date that recurrence or PD is objectively documented CR: at least 2 determinations of CR at least 4 weeks apart before progression where confirmation required or 1 determination of CR prior to progression where confirmation not required PR: at least 1 determination of PR or better at least 4 weeks apart before progression (& not qualifying for a CR) where confirmation required or 1 determination of PR prior to progression where confirmation not required PD: progression <= start of treatment (& not qualifying for CR, PR or SD) SD: at least 1 SD assessment (or better) > 6 weeks after randomization/start of treatment (& not qualifying for CR or PR)
irRC is a set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment, where the compound being evaluated is an immuno-oncology drug

End point type	Secondary

End point timeframe:

61 months

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis planned

End point values	ATC 400 mg/q4w	NSCLC 400 mg/q4w	Melanoma 400 mg/q4w	NSCLC 300 mg/q3w
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	11	19	5
Units: months				
median (confidence interval 90%)	22.1 (3.8 to 999)	5.6 (5.3 to 16.6)	32.0 (15.6 to 999)	10.9 (3.7 to 999)

Statistical analyses

No statistical analyses for this end point

Post-hoc: All Collected Deaths

End point title	All Collected Deaths

End point description:

On treatment deaths were collected from the start of treatment up tp 30 days after study drug discontinuation, for a maximum duration of 114.3 weeks for Phase I part (treatment duration ranged from 2 to 110.3 weeks) and a maximum duration of 194.9 weeks for Phase II part (treatment duration ranged from 0.6 tp 190.9 weeks).
Deaths post treatment survival follow up were collected after the on-treatment period up to approx. 63 months.

End point type	Post-hoc

End point timeframe:

On treatment deaths: approx. 114.3 weeks (Phase I) & 194.9 weeks (phase II), all deaths: approx. 63 months

End point values	Phase 1 Part	Phase 2 Part		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	261		
Units: Participants				
On-treatment deaths	8	35		
Total deaths	37	177		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On treatment deaths were collected from first patient first treatment up to 30 days after study drug discontinuation, for a maximum duration of 114.3 weeks for the Part I phase and for a maximum duration of 194.9 weeks for the Phase II part.

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	1 mg/kg q2w

Reporting group description:

Phase I Dose escalation cohort patients who took PDR001 1 mg/kg q2w

Reporting group title	3 mg/kg q2w

Reporting group description:

Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q2w

Reporting group title	10 mg/kg q2w

Reporting group description:

Phase I Dose escalation cohort patients who took PRD001 10 mg/kg q2w

Reporting group title	All Phase I q2w

Reporting group description:

Phase I dose Cohorts - All patients in Phase I who took PDR001 q2w

Reporting group title	3 mg/kg q4w

Reporting group description:

Phase I Dose escalation cohort patients who took PRD001 3 mg/kg q4w

Reporting group title	5 mg/kg q4w

Reporting group description:

Phase I Dose escalation cohort patients who took PRD001 5 mg/kg q4w

Reporting group title	All phase I q4w

Reporting group description:

Phase I dose Cohorts - All patients in Phase I who took PDR001 q4w

Reporting group title	All phase I patients

Reporting group description:

All patients in Phase I regardless of how they took PDR001

Reporting group title	NSCLC 400mg/q4w

Reporting group description:

Phase II: non-small cell cancer patients who took PDR001 400 mg/q4w

Reporting group title	Melanoma 400mg/q4w

Reporting group description:

Phase II: Melanoma patients who took PDR001 400 mg/q4w

Reporting group title	TNBC 400mg/q4w

Reporting group description:

Phase II: Triple negative breast cancer (TNBC) patients who took PDR001 400 mg/q4w

Reporting group title	NSCLC 300mg/q3w

Reporting group description:	
Phase II: non-small cell cancer patients who took PDR001 300 mg/q3w	
Reporting group title	ATC 400 mg/q4w
Reporting group description:	
Patients in Phase II with anaplastic thyroid cancer (ATC) who took PDR001 400 mg/q4w	
Reporting group title	All phase II patients
Reporting group description:	
All patients in Phase II regardless of how they took PDR001	

Serious adverse events	1 mg/kg q2w	3 mg/kg q2w	10 mg/kg q2w
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)	7 / 15 (46.67%)	4 / 11 (36.36%)
number of deaths (all causes)	2	2	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tumour haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of device insertion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (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
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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			
Pelvic pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 distress syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
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	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (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
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Tracheal stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
Depression			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (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
Mental status changes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Blood bilirubin increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 flutter			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery occlusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 pressure increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 11 (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
Lymphadenopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
Eye disorders			

Diplopia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 distension			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	0 / 11 (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 colitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
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 ulcer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (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
Ileus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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			
Dermatitis atopic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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			
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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			
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sjogren's syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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			
Bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (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
Empyema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (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			
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
Diabetic ketoacidosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (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
Failure to thrive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (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
Hyperkalaemia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
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	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All Phase I q2w	3 mg/kg q4w	5 mg/kg q4w
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 42 (47.62%)	2 / 6 (33.33%)	2 / 10 (20.00%)
number of deaths (all causes)	5	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metastases to central nervous system			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 inflammation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lymphorrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of device insertion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Fatigue			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Peripheral swelling			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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			
Pelvic pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 distress syndrome			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (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
Pneumonitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Tracheal stenosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Depression			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Mental status changes			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 flutter			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery occlusion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 pressure increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (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
Lymphadenopathy			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 distension			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Gastric ulcer			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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 haemorrhage			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (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
Ileus			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Melaena			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Hepatic failure			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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			
Dermatitis atopic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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			

Renal failure			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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			
Back pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sjogren's syndrome			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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			
Bacteraemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Empyema			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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			
Dehydration			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (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
Failure to thrive			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	2 / 42 (4.76%)	1 / 6 (16.67%)	0 / 10 (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
Hyperkalaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
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	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All phase I q4w	All phase I patients	NSCLC 400mg/q4w
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 16 (25.00%)	24 / 58 (41.38%)	27 / 59 (45.76%)
number of deaths (all causes)	3	8	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cancer pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypotension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of device insertion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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			
Pelvic pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 distress syndrome			

subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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	1 / 16 (6.25%)	2 / 58 (3.45%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (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
Obstructive airways disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			

subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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	1 / 16 (6.25%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (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
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Tracheal stenosis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Depression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Mental status changes			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tracheal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery occlusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			

subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 pressure increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	1 / 58 (1.72%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 distension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	3 / 58 (5.17%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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

Constipation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Gastric ulcer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (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
Ileus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (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
Melaena			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			

subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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			
Dermatitis atopic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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			
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sjogren's syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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			
Bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Empyema			

subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	2 / 58 (3.45%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
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 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (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
Failure to thrive			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (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
Hypercalcaemia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (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
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Melanoma 400mg/q4w	TNBC 400mg/q4w	NSCLC 300mg/q3w
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 61 (36.07%)	18 / 40 (45.00%)	37 / 59 (62.71%)
number of deaths (all causes)	4	4	12
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			

subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	0 / 59 (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
Tumour inflammation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	2 / 40 (5.00%)	0 / 59 (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
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Hypotension			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Lymphorrhoea			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Superior vena cava syndrome			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of device insertion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Pyrexia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchial obstruction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cough			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	1 / 61 (1.64%)	3 / 40 (7.50%)	7 / 59 (11.86%)
occurrences causally related to treatment / all	0 / 1	2 / 4	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 5
Haemoptysis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoxia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	5 / 40 (12.50%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tracheal stenosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Depression			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Blood bilirubin increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Wound dehiscence			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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 coronary syndrome			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arrhythmia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Atrial fibrillation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 flutter			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Cardiac tamponade			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tachycardia			

subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Carotid artery occlusion			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Central nervous system lesion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Facial paralysis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Hydrocephalus			

subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Seizure			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Diplopia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	2 / 40 (5.00%)	0 / 59 (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 colitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Ileus			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			

subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Bile duct obstruction			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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			
Renal failure			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	4 / 59 (6.78%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Sjogren's syndrome			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	0 / 59 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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 / 61 (0.00%)	0 / 40 (0.00%)	5 / 59 (8.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Postoperative wound infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			

subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (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
Sepsis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 61 (0.00%)	2 / 40 (5.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Hypercalcaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			

subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
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	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (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
Hypokalaemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ATC 400 mg/q4w	All phase II patients	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 42 (52.38%)	126 / 261 (48.28%)	
number of deaths (all causes)	11	35	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial tumour haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	

Metastases to central nervous system			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Second primary malignancy			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour inflammation			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypotension			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lymphorrhoea			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication of device insertion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Peripheral swelling			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchial obstruction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cough			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 42 (4.76%)	16 / 261 (6.13%)	
occurrences causally related to treatment / all	0 / 2	2 / 17	
deaths causally related to treatment / all	0 / 1	0 / 7	
Haemoptysis			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypoxia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pharyngeal haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pleural effusion			
subjects affected / exposed	2 / 42 (4.76%)	11 / 261 (4.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia aspiration			

subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Tracheal stenosis			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal obstruction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 42 (2.38%)	4 / 261 (1.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac tamponade			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tachycardia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			

subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic stroke			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Seizure			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			

subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune colitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	2 / 42 (4.76%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gastric ulcer			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 42 (0.00%)	6 / 261 (2.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sjogren's syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 42 (4.76%)	4 / 261 (1.53%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	3 / 42 (7.14%)	11 / 261 (4.21%)	
occurrences causally related to treatment / all	0 / 3	1 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Postoperative wound infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 42 (4.76%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypercalcaemia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	1 mg/kg q2w	3 mg/kg q2w	10 mg/kg q2w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	15 / 15 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tumour haemorrhage			

subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Tumour pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lymphoedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Chills			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Face oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	10 / 16 (62.50%)	3 / 15 (20.00%)	2 / 11 (18.18%)
occurrences (all)	10	4	2
Inflammation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	1	2	1
Oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	2 / 11 (18.18%)
occurrences (all)	1	3	2
Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	4	2	1
Swelling face			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 16 (18.75%)	4 / 15 (26.67%)	0 / 11 (0.00%)
occurrences (all)	5	5	0
Dyspnoea			
subjects affected / exposed	5 / 16 (31.25%)	7 / 15 (46.67%)	2 / 11 (18.18%)
occurrences (all)	9	9	3
Dyspnoea exertional			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	4	1	1
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Productive cough			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Agitation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hallucination			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	2	2	2
Bacterial test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 16 (18.75%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	4	3	0
Blood bilirubin increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Blood creatinine decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	3
Transaminases increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Weight decreased			

subjects affected / exposed	4 / 16 (25.00%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	4	2	1
Weight increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Joint dislocation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ligament rupture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Wound complication			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sinus tachycardia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	4 / 16 (25.00%)	6 / 15 (40.00%)	0 / 11 (0.00%)
occurrences (all)	5	8	0
Dysarthria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 16 (6.25%)	4 / 15 (26.67%)	1 / 11 (9.09%)
occurrences (all)	1	4	1
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Lethargy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Loss of consciousness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

Neuropathy peripheral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Paralysis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 16 (31.25%)	7 / 15 (46.67%)	2 / 11 (18.18%)
occurrences (all)	10	11	3
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Eosinophilia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lymph node pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Otorrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Photopsia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Abdominal pain			
subjects affected / exposed	3 / 16 (18.75%)	2 / 15 (13.33%)	2 / 11 (18.18%)
occurrences (all)	3	2	2
Abdominal pain lower			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Ascites			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Autoimmune colitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	5 / 16 (31.25%)	5 / 15 (33.33%)	0 / 11 (0.00%)
occurrences (all)	5	8	0
Diarrhoea			
subjects affected / exposed	7 / 16 (43.75%)	6 / 15 (40.00%)	1 / 11 (9.09%)
occurrences (all)	9	6	5
Dry mouth			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	3	1	1

Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Mouth haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	7 / 16 (43.75%)	4 / 15 (26.67%)	3 / 11 (27.27%)
occurrences (all)	8	4	4
Pancreatic duct dilatation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	6 / 16 (37.50%)	1 / 15 (6.67%)	3 / 11 (27.27%)
occurrences (all)	6	2	3

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cold sweat			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Lichen planus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	3 / 16 (18.75%)	5 / 15 (33.33%)	1 / 11 (9.09%)
occurrences (all)	4	5	1
Rash			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Rash erythematous			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vitiligo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Azotaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Hydronephrosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	3 / 16 (18.75%)	3 / 15 (20.00%)	1 / 11 (9.09%)
occurrences (all)	3	3	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	3 / 15 (20.00%)	1 / 11 (9.09%)
occurrences (all)	0	3	1
Back pain			
subjects affected / exposed	2 / 16 (12.50%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Groin pain			

subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Limb discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
Myalgia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Neck pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	2 / 11 (18.18%)
occurrences (all)	0	2	2
Pathological fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Acute sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Bacteraemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Fungal skin infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Laryngitis bacterial			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Otitis media			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Peritonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Postoperative wound infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	3 / 15 (20.00%)	0 / 11 (0.00%)
occurrences (all)	3	3	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	5 / 16 (31.25%)	1 / 15 (6.67%)	3 / 11 (27.27%)
occurrences (all)	5	1	3
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	0	3	3
Hyperglycaemia			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	9	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hypoglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	3	3	1
Hypomagnesaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	2 / 16 (12.50%)	3 / 15 (20.00%)	1 / 11 (9.09%)
occurrences (all)	4	3	1
Hypophosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	0	3	2

Non-serious adverse events	All Phase I q2w	3 mg/kg q4w	5 mg/kg q4w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)	6 / 6 (100.00%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tumour haemorrhage			

subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Tumour pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lymphoedema			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Chills			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Face oedema			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	15 / 42 (35.71%)	2 / 6 (33.33%)	5 / 10 (50.00%)
occurrences (all)	16	2	6
Inflammation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	4	0	1
Oedema			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	6	0	2
Pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	7	0	1
Swelling face			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 42 (16.67%)	0 / 6 (0.00%)	3 / 10 (30.00%)
occurrences (all)	10	0	3
Dyspnoea			
subjects affected / exposed	14 / 42 (33.33%)	0 / 6 (0.00%)	4 / 10 (40.00%)
occurrences (all)	21	0	4
Dyspnoea exertional			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hiccups			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	2 / 10 (20.00%)
occurrences (all)	6	0	4
Pneumonitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Respiratory tract congestion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tachypnoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Agitation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 42 (2.38%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Hallucination			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 6 (16.67%)	3 / 10 (30.00%)
occurrences (all)	1	1	3

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	6	0	1
Bacterial test positive			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	7	0	0
Blood bilirubin increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Blood creatinine decreased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Transaminases increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Weight decreased			

subjects affected / exposed	7 / 42 (16.67%)	1 / 6 (16.67%)	3 / 10 (30.00%)
occurrences (all)	7	1	3
Weight increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Joint dislocation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ligament rupture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	3 / 42 (7.14%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	4	1	0
Wound complication			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	10 / 42 (23.81%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	13	0	0
Dysarthria			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Headache			
subjects affected / exposed	6 / 42 (14.29%)	1 / 6 (16.67%)	3 / 10 (30.00%)
occurrences (all)	6	2	3
Hypoaesthesia			
subjects affected / exposed	2 / 42 (4.76%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Lethargy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Loss of consciousness			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Neuropathy peripheral			
subjects affected / exposed	1 / 42 (2.38%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Paraesthesia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Paralysis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 42 (33.33%)	1 / 6 (16.67%)	3 / 10 (30.00%)
occurrences (all)	24	1	3
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eosinophilia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lymph node pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Otorrhoea			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Photopsia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	2
Abdominal pain			
subjects affected / exposed	7 / 42 (16.67%)	2 / 6 (33.33%)	3 / 10 (30.00%)
occurrences (all)	7	5	4
Abdominal pain lower			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Ascites			
subjects affected / exposed	1 / 42 (2.38%)	2 / 6 (33.33%)	2 / 10 (20.00%)
occurrences (all)	1	2	2
Autoimmune colitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	10 / 42 (23.81%)	2 / 6 (33.33%)	0 / 10 (0.00%)
occurrences (all)	13	2	0
Diarrhoea			
subjects affected / exposed	14 / 42 (33.33%)	0 / 6 (0.00%)	3 / 10 (30.00%)
occurrences (all)	20	0	5
Dry mouth			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1

Dyspepsia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Dysphagia			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Flatulence			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Mouth haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	14 / 42 (33.33%)	3 / 6 (50.00%)	4 / 10 (40.00%)
occurrences (all)	16	4	4
Pancreatic duct dilatation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	10 / 42 (23.81%)	2 / 6 (33.33%)	2 / 10 (20.00%)
occurrences (all)	11	4	2

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cold sweat			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Lichen planus			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pain of skin			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Papule			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	9 / 42 (21.43%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	10	0	0
Rash			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Rash erythematous			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Skin ulcer			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vitiligo			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Azotaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	1 / 42 (2.38%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	1	0

Hydronephrosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Urinary incontinence			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	7 / 42 (16.67%)	0 / 6 (0.00%)	2 / 10 (20.00%)
occurrences (all)	7	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 42 (9.52%)	1 / 6 (16.67%)	2 / 10 (20.00%)
occurrences (all)	4	1	2
Back pain			
subjects affected / exposed	4 / 42 (9.52%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	4	1	0
Bone pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Groin pain			

subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Limb discomfort			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	3 / 42 (7.14%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Musculoskeletal pain			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	3	0	1
Myalgia			
subjects affected / exposed	3 / 42 (7.14%)	2 / 6 (33.33%)	0 / 10 (0.00%)
occurrences (all)	3	2	0
Neck pain			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Osteoarthritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	4 / 42 (9.52%)	1 / 6 (16.67%)	1 / 10 (10.00%)
occurrences (all)	4	1	2
Pathological fracture			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Acute sinusitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Bacteraemia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Fungal skin infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Laryngitis bacterial			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	2 / 42 (4.76%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Otitis media			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Peritonitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Postoperative wound infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Sinusitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	6	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	9 / 42 (21.43%)	2 / 6 (33.33%)	2 / 10 (20.00%)
occurrences (all)	9	2	2
Dehydration			
subjects affected / exposed	3 / 42 (7.14%)	2 / 6 (33.33%)	0 / 10 (0.00%)
occurrences (all)	3	2	0
Diabetes mellitus			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	3 / 42 (7.14%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	6	1	0
Hyperglycaemia			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	10	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Hypocalcaemia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Hypoglycaemia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Hypokalaemia			
subjects affected / exposed	4 / 42 (9.52%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	7	1	0
Hypomagnesaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	6 / 42 (14.29%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	8	0	1
Hypophosphataemia			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	2

Non-serious adverse events	All phase I q4w	All phase I patients	NSCLC 400mg/q4w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	58 / 58 (100.00%)	54 / 59 (91.53%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Tumour haemorrhage			

subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Tumour pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Lymphoedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	12 / 59 (20.34%)
occurrences (all)	0	2	12
Chills			
subjects affected / exposed	0 / 16 (0.00%)	4 / 58 (6.90%)	0 / 59 (0.00%)
occurrences (all)	0	4	0
Face oedema			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences (all)	1	2	1
Fatigue			
subjects affected / exposed	7 / 16 (43.75%)	22 / 58 (37.93%)	11 / 59 (18.64%)
occurrences (all)	8	24	12
Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	4 / 59 (6.78%)
occurrences (all)	0	2	4
Non-cardiac chest pain			
subjects affected / exposed	1 / 16 (6.25%)	5 / 58 (8.62%)	2 / 59 (3.39%)
occurrences (all)	1	5	3
Oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)	6 / 58 (10.34%)	5 / 59 (8.47%)
occurrences (all)	2	8	5
Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Peripheral swelling			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	6 / 58 (10.34%)	9 / 59 (15.25%)
occurrences (all)	1	8	13
Swelling face			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Seasonal allergy			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 16 (18.75%)	10 / 58 (17.24%)	13 / 59 (22.03%)
occurrences (all)	3	13	18
Dyspnoea			
subjects affected / exposed	4 / 16 (25.00%)	18 / 58 (31.03%)	17 / 59 (28.81%)
occurrences (all)	4	25	17
Dyspnoea exertional			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Hiccups			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Hypoxia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Pleural effusion			
subjects affected / exposed	2 / 16 (12.50%)	7 / 58 (12.07%)	3 / 59 (5.08%)
occurrences (all)	4	10	3
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	4
Productive cough			

subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	6 / 59 (10.17%)
occurrences (all)	1	2	6
Respiratory tract congestion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Tachypnoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract congestion			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Agitation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	2 / 59 (3.39%)
occurrences (all)	1	2	2
Hallucination			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	4 / 16 (25.00%)	5 / 58 (8.62%)	2 / 59 (3.39%)
occurrences (all)	4	5	2

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	2 / 59 (3.39%)
occurrences (all)	1	4	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	6 / 58 (10.34%)	3 / 59 (5.08%)
occurrences (all)	1	7	3
Bacterial test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)	5 / 58 (8.62%)	2 / 59 (3.39%)
occurrences (all)	0	7	2
Blood bilirubin increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Blood creatinine decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences (all)	1	4	1
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Transaminases increased			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	0 / 59 (0.00%)
occurrences (all)	1	3	0
Weight decreased			

subjects affected / exposed	4 / 16 (25.00%)	11 / 58 (18.97%)	6 / 59 (10.17%)
occurrences (all)	4	11	6
Weight increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Joint dislocation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Ligament rupture			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Post-traumatic pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Procedural pain			
subjects affected / exposed	1 / 16 (6.25%)	4 / 58 (6.90%)	1 / 59 (1.69%)
occurrences (all)	1	5	1
Wound complication			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Tachycardia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences (all)	1	2	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	10 / 58 (17.24%)	1 / 59 (1.69%)
occurrences (all)	0	13	1
Dysarthria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences (all)	1	3	1
Headache			
subjects affected / exposed	4 / 16 (25.00%)	10 / 58 (17.24%)	4 / 59 (6.78%)
occurrences (all)	5	11	5
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences (all)	1	3	1
Lethargy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Loss of consciousness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0

Neuropathy peripheral			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Paralysis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Presyncope			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Taste disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 16 (25.00%)	18 / 58 (31.03%)	16 / 59 (27.12%)
occurrences (all)	4	28	18
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Eosinophilia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Iron deficiency anaemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Leukopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Lymph node pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Otorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Photopsia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)	4 / 58 (6.90%)	1 / 59 (1.69%)
occurrences (all)	2	5	1
Abdominal pain			
subjects affected / exposed	5 / 16 (31.25%)	12 / 58 (20.69%)	3 / 59 (5.08%)
occurrences (all)	9	16	3
Abdominal pain lower			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences (all)	0	3	1
Ascites			
subjects affected / exposed	4 / 16 (25.00%)	5 / 58 (8.62%)	0 / 59 (0.00%)
occurrences (all)	4	5	0
Autoimmune colitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 16 (12.50%)	12 / 58 (20.69%)	8 / 59 (13.56%)
occurrences (all)	2	15	10
Diarrhoea			
subjects affected / exposed	3 / 16 (18.75%)	17 / 58 (29.31%)	8 / 59 (13.56%)
occurrences (all)	5	25	17
Dry mouth			
subjects affected / exposed	1 / 16 (6.25%)	6 / 58 (10.34%)	3 / 59 (5.08%)
occurrences (all)	1	6	3

Dyspepsia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	2 / 59 (3.39%)
occurrences (all)	1	2	2
Dysphagia			
subjects affected / exposed	0 / 16 (0.00%)	3 / 58 (5.17%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences (all)	0	3	1
Mouth haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Nausea			
subjects affected / exposed	7 / 16 (43.75%)	21 / 58 (36.21%)	9 / 59 (15.25%)
occurrences (all)	8	24	10
Pancreatic duct dilatation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	4 / 16 (25.00%)	14 / 58 (24.14%)	8 / 59 (13.56%)
occurrences (all)	6	17	10

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Cold sweat			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Lichen planus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Night sweats			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Pain of skin			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	9 / 58 (15.52%)	7 / 59 (11.86%)
occurrences (all)	0	10	7
Rash			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	5 / 59 (8.47%)
occurrences (all)	0	2	5
Rash erythematous			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 16 (0.00%)	3 / 58 (5.17%)	2 / 59 (3.39%)
occurrences (all)	0	3	2
Skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Vitiligo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Azotaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	1	2	0

Hydronephrosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Micturition urgency			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Pollakiuria			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Urinary incontinence			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	5 / 59 (8.47%)
occurrences (all)	0	0	5
Hypothyroidism			
subjects affected / exposed	2 / 16 (12.50%)	9 / 58 (15.52%)	4 / 59 (6.78%)
occurrences (all)	2	9	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 16 (18.75%)	7 / 58 (12.07%)	8 / 59 (13.56%)
occurrences (all)	3	7	9
Back pain			
subjects affected / exposed	1 / 16 (6.25%)	5 / 58 (8.62%)	8 / 59 (13.56%)
occurrences (all)	1	5	10
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	5
Coccydynia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Flank pain			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	1 / 59 (1.69%)
occurrences (all)	1	3	1
Groin pain			

subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Limb discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	2 / 59 (3.39%)
occurrences (all)	0	2	2
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)	4 / 58 (6.90%)	1 / 59 (1.69%)
occurrences (all)	1	4	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal pain			
subjects affected / exposed	1 / 16 (6.25%)	4 / 58 (6.90%)	5 / 59 (8.47%)
occurrences (all)	1	4	7
Myalgia			
subjects affected / exposed	2 / 16 (12.50%)	5 / 58 (8.62%)	4 / 59 (6.78%)
occurrences (all)	2	5	5
Neck pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Osteoarthritis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	2 / 16 (12.50%)	6 / 58 (10.34%)	1 / 59 (1.69%)
occurrences (all)	3	7	1
Pathological fracture			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0

Acute sinusitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Fungal skin infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 58 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	4
Laryngitis bacterial			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	2 / 59 (3.39%)
occurrences (all)	0	1	3
Oral candidiasis			
subjects affected / exposed	1 / 16 (6.25%)	3 / 58 (5.17%)	0 / 59 (0.00%)
occurrences (all)	1	3	0
Otitis media			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Peritonitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	3 / 58 (5.17%)	3 / 59 (5.08%)
occurrences (all)	0	3	4
Postoperative wound infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0

Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	4 / 58 (6.90%)	2 / 59 (3.39%)
occurrences (all)	0	6	2
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	4 / 16 (25.00%)	13 / 58 (22.41%)	18 / 59 (30.51%)
occurrences (all)	4	13	19
Dehydration			
subjects affected / exposed	2 / 16 (12.50%)	5 / 58 (8.62%)	0 / 59 (0.00%)
occurrences (all)	2	5	0
Diabetes mellitus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Hypercalcaemia			
subjects affected / exposed	1 / 16 (6.25%)	4 / 58 (6.90%)	4 / 59 (6.78%)
occurrences (all)	1	7	4
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	4 / 58 (6.90%)	1 / 59 (1.69%)
occurrences (all)	0	10	1
Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 58 (1.72%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Hypernatraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	3 / 59 (5.08%)
occurrences (all)	0	4	9
Hypocalcaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 58 (3.45%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)	5 / 58 (8.62%)	2 / 59 (3.39%)
occurrences (all)	1	8	4
Hypomagnesaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 58 (1.72%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 16 (6.25%)	7 / 58 (12.07%)	2 / 59 (3.39%)
occurrences (all)	1	9	2
Hypophosphataemia			
subjects affected / exposed	1 / 16 (6.25%)	4 / 58 (6.90%)	3 / 59 (5.08%)
occurrences (all)	2	7	15

Non-serious adverse events	Melanoma 400mg/q4w	TNBC 400mg/q4w	NSCLC 300mg/q3w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 61 (90.16%)	37 / 40 (92.50%)	56 / 59 (94.92%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	5 / 59 (8.47%)
occurrences (all)	2	0	5
Tumour haemorrhage			

subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Tumour pain			
subjects affected / exposed	1 / 61 (1.64%)	6 / 40 (15.00%)	0 / 59 (0.00%)
occurrences (all)	1	6	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 61 (0.00%)	2 / 40 (5.00%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Hot flush			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Hypotension			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Lymphoedema			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 61 (13.11%)	4 / 40 (10.00%)	12 / 59 (20.34%)
occurrences (all)	11	4	17
Chills			
subjects affected / exposed	1 / 61 (1.64%)	2 / 40 (5.00%)	2 / 59 (3.39%)
occurrences (all)	1	2	2
Face oedema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	12 / 61 (19.67%)	13 / 40 (32.50%)	12 / 59 (20.34%)
occurrences (all)	12	14	12
Inflammation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			

subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	3 / 61 (4.92%)	2 / 40 (5.00%)	8 / 59 (13.56%)
occurrences (all)	3	2	14
Oedema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	3 / 61 (4.92%)	5 / 40 (12.50%)	4 / 59 (6.78%)
occurrences (all)	4	7	4
Pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences (all)	1	0	2
Peripheral swelling			
subjects affected / exposed	3 / 61 (4.92%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	9 / 61 (14.75%)	3 / 40 (7.50%)	11 / 59 (18.64%)
occurrences (all)	11	3	26
Swelling face			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Vulvovaginal pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 61 (13.11%)	10 / 40 (25.00%)	20 / 59 (33.90%)
occurrences (all)	10	10	22
Dyspnoea			
subjects affected / exposed	1 / 61 (1.64%)	10 / 40 (25.00%)	18 / 59 (30.51%)
occurrences (all)	2	10	18
Dyspnoea exertional			
subjects affected / exposed	0 / 61 (0.00%)	2 / 40 (5.00%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Haemoptysis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences (all)	1	0	3
Hiccups			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Pleural effusion			
subjects affected / exposed	1 / 61 (1.64%)	4 / 40 (10.00%)	3 / 59 (5.08%)
occurrences (all)	1	4	5
Pneumonitis			
subjects affected / exposed	3 / 61 (4.92%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	4	0	0
Productive cough			

subjects affected / exposed	1 / 61 (1.64%)	3 / 40 (7.50%)	2 / 59 (3.39%)
occurrences (all)	1	3	4
Respiratory tract congestion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	0 / 61 (0.00%)	2 / 40 (5.00%)	3 / 59 (5.08%)
occurrences (all)	0	2	3
Confusional state			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Hallucination			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	6 / 61 (9.84%)	4 / 40 (10.00%)	5 / 59 (8.47%)
occurrences (all)	6	4	6

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 61 (11.48%)	5 / 40 (12.50%)	5 / 59 (8.47%)
occurrences (all)	7	7	7
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 61 (11.48%)	8 / 40 (20.00%)	5 / 59 (8.47%)
occurrences (all)	7	10	6
Bacterial test positive			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 61 (3.28%)	6 / 40 (15.00%)	3 / 59 (5.08%)
occurrences (all)	2	6	3
Blood bilirubin increased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	3 / 59 (5.08%)
occurrences (all)	4	0	4
Blood creatinine decreased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	4 / 61 (6.56%)	1 / 40 (2.50%)	4 / 59 (6.78%)
occurrences (all)	9	1	8
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 61 (1.64%)	2 / 40 (5.00%)	3 / 59 (5.08%)
occurrences (all)	1	2	3
Lymphocyte count decreased			
subjects affected / exposed	3 / 61 (4.92%)	2 / 40 (5.00%)	0 / 59 (0.00%)
occurrences (all)	3	2	0
Transaminases increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Weight decreased			

subjects affected / exposed	5 / 61 (8.20%)	2 / 40 (5.00%)	9 / 59 (15.25%)
occurrences (all)	6	2	10
Weight increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
White blood cell count decreased			
subjects affected / exposed	3 / 61 (4.92%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	5	0	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Joint dislocation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Ligament rupture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Wound complication			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			

subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	1	1	2
Tachycardia			
subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Aphasia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	5 / 61 (8.20%)	4 / 40 (10.00%)	10 / 59 (16.95%)
occurrences (all)	5	4	10
Dysarthria			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	4 / 61 (6.56%)	2 / 40 (5.00%)	7 / 59 (11.86%)
occurrences (all)	4	2	8
Hypoaesthesia			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Lethargy			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Loss of consciousness			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0

Neuropathy peripheral			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	4
Paralysis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	2
Taste disorder			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 61 (21.31%)	6 / 40 (15.00%)	8 / 59 (13.56%)
occurrences (all)	17	7	10
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			

subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Lymph node pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	3 / 61 (4.92%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	3	1	1
Neutropenia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	2 / 61 (3.28%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	3	1	3
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Otorrhoea			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Photopsia			

subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	2 / 61 (3.28%)	5 / 40 (12.50%)	5 / 59 (8.47%)
occurrences (all)	2	5	5
Abdominal pain lower			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences (all)	1	0	2
Ascites			
subjects affected / exposed	0 / 61 (0.00%)	2 / 40 (5.00%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Autoimmune colitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	7 / 61 (11.48%)	9 / 40 (22.50%)	9 / 59 (15.25%)
occurrences (all)	7	9	9
Diarrhoea			
subjects affected / exposed	8 / 61 (13.11%)	1 / 40 (2.50%)	12 / 59 (20.34%)
occurrences (all)	11	1	27
Dry mouth			
subjects affected / exposed	3 / 61 (4.92%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	3	1	0

Dyspepsia			
subjects affected / exposed	3 / 61 (4.92%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	3	0	1
Dysphagia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Flatulence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	6 / 61 (9.84%)	13 / 40 (32.50%)	15 / 59 (25.42%)
occurrences (all)	6	14	17
Pancreatic duct dilatation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 61 (1.64%)	2 / 40 (5.00%)	1 / 59 (1.69%)
occurrences (all)	2	2	1
Toothache			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	8 / 61 (13.11%)	5 / 40 (12.50%)	8 / 59 (13.56%)
occurrences (all)	9	5	14

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Cold sweat			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	2 / 61 (3.28%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Hyperhidrosis			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Lichen planus			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Pain of skin			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	8 / 61 (13.11%)	4 / 40 (10.00%)	3 / 59 (5.08%)
occurrences (all)	10	4	4
Rash			
subjects affected / exposed	6 / 61 (9.84%)	3 / 40 (7.50%)	3 / 59 (5.08%)
occurrences (all)	7	3	5
Rash erythematous			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	3 / 61 (4.92%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	5	0	2
Skin ulcer			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Vitiligo			
subjects affected / exposed	10 / 61 (16.39%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	10	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Azotaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	1	1	5
Haematuria			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0

Hydronephrosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	4 / 61 (6.56%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	4	1	2
Hypothyroidism			
subjects affected / exposed	5 / 61 (8.20%)	3 / 40 (7.50%)	3 / 59 (5.08%)
occurrences (all)	6	3	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 61 (11.48%)	0 / 40 (0.00%)	6 / 59 (10.17%)
occurrences (all)	8	0	6
Back pain			
subjects affected / exposed	1 / 61 (1.64%)	3 / 40 (7.50%)	10 / 59 (16.95%)
occurrences (all)	1	4	11
Bone pain			
subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	3 / 59 (5.08%)
occurrences (all)	2	0	3
Coccydynia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	2 / 61 (3.28%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	2	1	0
Groin pain			

subjects affected / exposed	2 / 61 (3.28%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Limb discomfort			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Muscular weakness			
subjects affected / exposed	4 / 61 (6.56%)	3 / 40 (7.50%)	1 / 59 (1.69%)
occurrences (all)	4	3	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 61 (3.28%)	2 / 40 (5.00%)	2 / 59 (3.39%)
occurrences (all)	2	2	2
Musculoskeletal pain			
subjects affected / exposed	1 / 61 (1.64%)	1 / 40 (2.50%)	9 / 59 (15.25%)
occurrences (all)	1	1	13
Myalgia			
subjects affected / exposed	4 / 61 (6.56%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	5	1	1
Neck pain			
subjects affected / exposed	2 / 61 (3.28%)	1 / 40 (2.50%)	3 / 59 (5.08%)
occurrences (all)	2	1	3
Osteoarthritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	4 / 61 (6.56%)	3 / 40 (7.50%)	4 / 59 (6.78%)
occurrences (all)	4	3	5
Pathological fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0

Acute sinusitis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Bacteraemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Laryngitis bacterial			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Oral candidiasis			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Otitis media			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Peritonitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	4
Postoperative wound infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0

Sinusitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	8 / 61 (13.11%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences (all)	9	0	2
Urinary tract infection			
subjects affected / exposed	2 / 61 (3.28%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	2	2	4
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	13 / 61 (21.31%)	7 / 40 (17.50%)	17 / 59 (28.81%)
occurrences (all)	13	7	23
Dehydration			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Diabetes mellitus			
subjects affected / exposed	1 / 61 (1.64%)	0 / 40 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	2
Hypercalcaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	3
Hyperglycaemia			
subjects affected / exposed	4 / 61 (6.56%)	1 / 40 (2.50%)	3 / 59 (5.08%)
occurrences (all)	6	2	4
Hyperkalaemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	0	1	2
Hypernatraemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			

subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 61 (3.28%)	3 / 40 (7.50%)	4 / 59 (6.78%)
occurrences (all)	3	3	9
Hypocalcaemia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 40 (2.50%)	2 / 59 (3.39%)
occurrences (all)	0	1	3
Hypoglycaemia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 40 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	3 / 61 (4.92%)	2 / 40 (5.00%)	6 / 59 (10.17%)
occurrences (all)	3	3	6
Hypomagnesaemia			
subjects affected / exposed	2 / 61 (3.28%)	2 / 40 (5.00%)	3 / 59 (5.08%)
occurrences (all)	2	3	5
Hyponatraemia			
subjects affected / exposed	3 / 61 (4.92%)	4 / 40 (10.00%)	2 / 59 (3.39%)
occurrences (all)	3	4	2
Hypophosphataemia			
subjects affected / exposed	4 / 61 (6.56%)	1 / 40 (2.50%)	1 / 59 (1.69%)
occurrences (all)	7	1	2

Non-serious adverse events	ATC 400 mg/q4w	All phase II patients	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 42 (92.86%)	241 / 261 (92.34%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)	8 / 261 (3.07%)	
occurrences (all)	0	8	
Tumour haemorrhage			

subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Tumour pain			
subjects affected / exposed	3 / 42 (7.14%)	10 / 261 (3.83%)	
occurrences (all)	4	11	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Hot flush			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences (all)	0	3	
Hypotension			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences (all)	1	3	
Lymphoedema			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 42 (19.05%)	44 / 261 (16.86%)	
occurrences (all)	8	52	
Chills			
subjects affected / exposed	1 / 42 (2.38%)	6 / 261 (2.30%)	
occurrences (all)	1	6	
Face oedema			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Fatigue			
subjects affected / exposed	6 / 42 (14.29%)	54 / 261 (20.69%)	
occurrences (all)	7	57	
Inflammation			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences (all)	1	1	
Influenza like illness			

subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Malaise			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	4	
Non-cardiac chest pain			
subjects affected / exposed	0 / 42 (0.00%)	15 / 261 (5.75%)	
occurrences (all)	0	22	
Oedema			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	7 / 42 (16.67%)	24 / 261 (9.20%)	
occurrences (all)	8	28	
Pain			
subjects affected / exposed	1 / 42 (2.38%)	5 / 261 (1.92%)	
occurrences (all)	1	5	
Peripheral swelling			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	9 / 42 (21.43%)	41 / 261 (15.71%)	
occurrences (all)	13	66	
Swelling face			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Seasonal allergy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Vulvovaginal pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 42 (14.29%)	57 / 261 (21.84%)	
occurrences (all)	6	66	
Dyspnoea			
subjects affected / exposed	9 / 42 (21.43%)	55 / 261 (21.07%)	
occurrences (all)	10	57	
Dyspnoea exertional			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Haemoptysis			
subjects affected / exposed	4 / 42 (9.52%)	9 / 261 (3.45%)	
occurrences (all)	6	12	
Hiccups			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Hypoxia			
subjects affected / exposed	1 / 42 (2.38%)	4 / 261 (1.53%)	
occurrences (all)	1	4	
Oropharyngeal pain			
subjects affected / exposed	4 / 42 (9.52%)	9 / 261 (3.45%)	
occurrences (all)	4	9	
Pleural effusion			
subjects affected / exposed	1 / 42 (2.38%)	12 / 261 (4.60%)	
occurrences (all)	1	14	
Pneumonitis			
subjects affected / exposed	0 / 42 (0.00%)	6 / 261 (2.30%)	
occurrences (all)	0	8	
Productive cough			

subjects affected / exposed	3 / 42 (7.14%)	15 / 261 (5.75%)	
occurrences (all)	3	17	
Respiratory tract congestion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Sinus congestion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Tachypnoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract congestion			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	2 / 42 (4.76%)	4 / 261 (1.53%)	
occurrences (all)	2	4	
Anxiety			
subjects affected / exposed	2 / 42 (4.76%)	8 / 261 (3.07%)	
occurrences (all)	2	8	
Confusional state			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Depression			
subjects affected / exposed	2 / 42 (4.76%)	7 / 261 (2.68%)	
occurrences (all)	2	7	
Hallucination			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	2 / 42 (4.76%)	19 / 261 (7.28%)	
occurrences (all)	2	20	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 42 (7.14%)	22 / 261 (8.43%)	
occurrences (all)	4	27	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 42 (4.76%)	25 / 261 (9.58%)	
occurrences (all)	2	28	
Bacterial test positive			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 42 (2.38%)	14 / 261 (5.36%)	
occurrences (all)	1	14	
Blood bilirubin increased			
subjects affected / exposed	1 / 42 (2.38%)	5 / 261 (1.92%)	
occurrences (all)	1	9	
Blood creatinine decreased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	0 / 42 (0.00%)	10 / 261 (3.83%)	
occurrences (all)	0	19	
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	8 / 261 (3.07%)	
occurrences (all)	1	8	
Lymphocyte count decreased			
subjects affected / exposed	0 / 42 (0.00%)	5 / 261 (1.92%)	
occurrences (all)	0	5	
Transaminases increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Weight decreased			

subjects affected / exposed	2 / 42 (4.76%)	24 / 261 (9.20%)	
occurrences (all)	2	26	
Weight increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	2	
White blood cell count decreased			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	7	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Joint dislocation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Ligament rupture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Post-traumatic pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Wound complication			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences (all)	1	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Sinus tachycardia			

subjects affected / exposed	1 / 42 (2.38%)	6 / 261 (2.30%)	
occurrences (all)	1	6	
Tachycardia			
subjects affected / exposed	1 / 42 (2.38%)	5 / 261 (1.92%)	
occurrences (all)	1	5	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences (all)	0	3	
Aphasia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	3 / 42 (7.14%)	23 / 261 (8.81%)	
occurrences (all)	4	24	
Dysarthria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	5 / 42 (11.90%)	22 / 261 (8.43%)	
occurrences (all)	5	24	
Hypoaesthesia			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences (all)	0	3	
Lethargy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Loss of consciousness			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	

Neuropathy peripheral			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	1 / 42 (2.38%)	6 / 261 (2.30%)	
occurrences (all)	1	6	
Paralysis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences (all)	1	3	
Presyncope			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	3	
Taste disorder			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 42 (26.19%)	54 / 261 (20.69%)	
occurrences (all)	13	65	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Eosinophilia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Iron deficiency anaemia			

subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Leukocytosis			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences (all)	1	1	
Leukopenia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Lymph node pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Lymphopenia			
subjects affected / exposed	1 / 42 (2.38%)	7 / 261 (2.68%)	
occurrences (all)	1	7	
Neutropenia			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Thrombocytopenia			
subjects affected / exposed	1 / 42 (2.38%)	6 / 261 (2.30%)	
occurrences (all)	1	8	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Otorrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Vertigo			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences (all)	1	3	
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Photopsia			

subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	1 / 42 (2.38%)	4 / 261 (1.53%)	
occurrences (all)	1	4	
Abdominal pain			
subjects affected / exposed	3 / 42 (7.14%)	18 / 261 (6.90%)	
occurrences (all)	3	18	
Abdominal pain lower			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	4	
Ascites			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Autoimmune colitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	5 / 42 (11.90%)	38 / 261 (14.56%)	
occurrences (all)	5	40	
Diarrhoea			
subjects affected / exposed	8 / 42 (19.05%)	37 / 261 (14.18%)	
occurrences (all)	13	69	
Dry mouth			
subjects affected / exposed	3 / 42 (7.14%)	10 / 261 (3.83%)	
occurrences (all)	3	10	

Dyspepsia			
subjects affected / exposed	1 / 42 (2.38%)	7 / 261 (2.68%)	
occurrences (all)	1	7	
Dysphagia			
subjects affected / exposed	5 / 42 (11.90%)	8 / 261 (3.07%)	
occurrences (all)	5	8	
Flatulence			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Mouth haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences (all)	1	1	
Mouth ulceration			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	2 / 42 (4.76%)	45 / 261 (17.24%)	
occurrences (all)	2	49	
Pancreatic duct dilatation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	1 / 42 (2.38%)	6 / 261 (2.30%)	
occurrences (all)	1	7	
Toothache			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	3 / 42 (7.14%)	32 / 261 (12.26%)	
occurrences (all)	4	42	

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Cold sweat			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Dermatitis contact			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	4	
Hyperhidrosis			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	4	
Lichen planus			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Night sweats			
subjects affected / exposed	1 / 42 (2.38%)	4 / 261 (1.53%)	
occurrences (all)	1	4	
Pain of skin			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Papule			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	5 / 42 (11.90%)	27 / 261 (10.34%)	
occurrences (all)	6	31	
Rash			
subjects affected / exposed	3 / 42 (7.14%)	20 / 261 (7.66%)	
occurrences (all)	3	23	
Rash erythematous			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 42 (2.38%)	7 / 261 (2.68%)	
occurrences (all)	1	10	
Skin ulcer			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Vitiligo			
subjects affected / exposed	1 / 42 (2.38%)	11 / 261 (4.21%)	
occurrences (all)	1	11	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences (all)	1	3	
Azotaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	1 / 42 (2.38%)	5 / 261 (1.92%)	
occurrences (all)	1	8	
Haematuria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	

Hydronephrosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Micturition urgency			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 42 (2.38%)	13 / 261 (4.98%)	
occurrences (all)	1	13	
Hypothyroidism			
subjects affected / exposed	2 / 42 (4.76%)	17 / 261 (6.51%)	
occurrences (all)	2	18	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 42 (14.29%)	27 / 261 (10.34%)	
occurrences (all)	6	29	
Back pain			
subjects affected / exposed	5 / 42 (11.90%)	27 / 261 (10.34%)	
occurrences (all)	6	32	
Bone pain			
subjects affected / exposed	0 / 42 (0.00%)	8 / 261 (3.07%)	
occurrences (all)	0	10	
Coccydynia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	4	
Groin pain			

subjects affected / exposed	0 / 42 (0.00%)	2 / 261 (0.77%)	
occurrences (all)	0	2	
Limb discomfort			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 42 (0.00%)	4 / 261 (1.53%)	
occurrences (all)	0	4	
Muscular weakness			
subjects affected / exposed	1 / 42 (2.38%)	10 / 261 (3.83%)	
occurrences (all)	2	11	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 42 (4.76%)	8 / 261 (3.07%)	
occurrences (all)	2	8	
Musculoskeletal pain			
subjects affected / exposed	3 / 42 (7.14%)	19 / 261 (7.28%)	
occurrences (all)	3	25	
Myalgia			
subjects affected / exposed	3 / 42 (7.14%)	13 / 261 (4.98%)	
occurrences (all)	3	15	
Neck pain			
subjects affected / exposed	4 / 42 (9.52%)	10 / 261 (3.83%)	
occurrences (all)	4	10	
Osteoarthritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 42 (0.00%)	12 / 261 (4.60%)	
occurrences (all)	0	13	
Pathological fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences (all)	1	1	

Acute sinusitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	2	
Bacteraemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Fungal skin infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 42 (2.38%)	6 / 261 (2.30%)	
occurrences (all)	1	6	
Laryngitis bacterial			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	2 / 42 (4.76%)	6 / 261 (2.30%)	
occurrences (all)	3	8	
Oral candidiasis			
subjects affected / exposed	1 / 42 (2.38%)	3 / 261 (1.15%)	
occurrences (all)	1	4	
Otitis media			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Peritonitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	3 / 42 (7.14%)	10 / 261 (3.83%)	
occurrences (all)	3	12	
Postoperative wound infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 42 (2.38%)	1 / 261 (0.38%)	
occurrences (all)	1	1	

Sinusitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	13 / 261 (4.98%)	
occurrences (all)	0	14	
Urinary tract infection			
subjects affected / exposed	0 / 42 (0.00%)	7 / 261 (2.68%)	
occurrences (all)	0	10	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	5 / 42 (11.90%)	60 / 261 (22.99%)	
occurrences (all)	6	68	
Dehydration			
subjects affected / exposed	1 / 42 (2.38%)	2 / 261 (0.77%)	
occurrences (all)	1	2	
Diabetes mellitus			
subjects affected / exposed	0 / 42 (0.00%)	3 / 261 (1.15%)	
occurrences (all)	0	4	
Hypercalcaemia			
subjects affected / exposed	3 / 42 (7.14%)	9 / 261 (3.45%)	
occurrences (all)	5	12	
Hyperglycaemia			
subjects affected / exposed	2 / 42 (4.76%)	11 / 261 (4.21%)	
occurrences (all)	3	16	
Hyperkalaemia			
subjects affected / exposed	1 / 42 (2.38%)	4 / 261 (1.53%)	
occurrences (all)	1	5	
Hypernatraemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Hyperphosphataemia			

subjects affected / exposed	0 / 42 (0.00%)	1 / 261 (0.38%)	
occurrences (all)	0	1	
Hyperuricaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	2 / 42 (4.76%)	14 / 261 (5.36%)	
occurrences (all)	2	26	
Hypocalcaemia			
subjects affected / exposed	5 / 42 (11.90%)	8 / 261 (3.07%)	
occurrences (all)	6	10	
Hypoglycaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 261 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	4 / 42 (9.52%)	17 / 261 (6.51%)	
occurrences (all)	11	27	
Hypomagnesaemia			
subjects affected / exposed	3 / 42 (7.14%)	10 / 261 (3.83%)	
occurrences (all)	4	14	
Hyponatraemia			
subjects affected / exposed	3 / 42 (7.14%)	14 / 261 (5.36%)	
occurrences (all)	3	14	
Hypophosphataemia			
subjects affected / exposed	2 / 42 (4.76%)	11 / 261 (4.21%)	
occurrences (all)	2	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2015	Reduced the starting dose of spartalizumab to 1 mg/kg administered once every two weeks, as requested by a regulatory authority.
15 June 2015	Phase II part of the study was to focus specifically on subjects with NSCLC, melanoma and TNBC; the planned expansion groups for subjects with gastric and esophageal cancer, colorectal cancer and anal cancer were removed. Removal of the gastric/esophageal, colorectal and anal cancer groups also affects the role of the PD-L1 biomarker, which was an inclusion criterion for these subjects. No molecular screening for PD-L1 was performed to select subjects however PD-L1 expression was assessed retrospectively for all subjects. At the time of RP2D/MTD determination, the amount of efficacy data collected would be limited. To provide greater confidence in choosing the most appropriate dose for further development, the study design was updated to allow testing of two doses of spartalizumab in one disease indication during the Phase II part. In addition, collection of a sample for cytokine assessment (IL-6 and IFN-γ) was added for all subjects at Screening. The wording in prohibited concomitant therapy related to the use of systemic steroid therapy during the course of study was adjusted in order to provide more flexibility for subjects who would need such therapy for treatment of acute conditions. In order to align the collection and analysis of pharmacodynamic biomarkers with preclinical evidence on the timing of immune response in tumor after therapy with PD-1 blocking antibodies, the collection of the on-treatment new tumor biopsy sample was moved from C2D1 (i.e. between C2D1 and C2D15) to C3D1 (i.e. between C3D1 and C3D15).
19 September 2015	Restricting subjects with NSCLC to no more than one prior platinum-based doublet chemotherapy regimen, with the exception of subjects with ALK or EGFR-positive disease who were treated with a relevant tyrosine kinase inhibitor and a platinum-based doublet chemotherapy regimen. For subjects with melanoma, all subjects must have developed progressive disease after at least one systemic treatment regimen (for those with BRAF-wild type disease) or one systemic treatment regimen and a BRAF inhibitor (for those with BRAF-mutant disease). No disease-specific limitations were required for subjects with TNBC. Subjects who had previously received a PD-1 or PD-L1 checkpoint inhibitor were excluded from participating; those who had previously received other anticancer immunotherapies such as CTLA-4-directed therapy were eligible. Allowed the testing of a fixed/flat dose of spartalizumab in the phase II part of the study. The use of a fixed/flat dose would reduce the risk of dosing errors and reduce drug product wastage. The requirement that subjects have disease that could be biopsied and be willing to undergo biopsy during the Phase II part of the study was adjusted to allow exceptions after documented discussion with Novartis. This amendment also introduced the possibility to stop the collection of biopsies, once a sufficient number of paired biopsies had been collected. Allowed the collection of tumor tissue upon the development of acquired resistance to treatment. Based on preliminary PK data and the possibility of delayed appearance of immune-related adverse events, the safety follow-up period was extended to 90 days after the last dose of study treatment. Exclusion criteria were updated to exclude sexually active male subjects who were not willing to use a condom during the study.

13 May 2016	n the Phase II part. This regimen was to be tested in addition to the RP2D of 400 mg Q4W. Subjects with melanoma were no longer required to have received systemic therapy prior to being eligible for treatment with spartalizumab. All subjects with BRAF V600 mutant melanoma must have received a BRAF inhibitor. Subjects with NSCLC could have received no more than one prior platinum-based doublet therapy. For NSCLC, the subjects with EGFR mutation-positive disease were excluded as the published data suggest these subjects receive limited benefit from treatment with single agent PD-1 inhibitors (Borghaei et al 2015). Subjects with ALK translocation-positive NSCLC were eligible, as the currently available published dataset for these subjects treated with PD-1 inhibitors is limited. A group of subjects was added with anaplastic thyroid cancer in the Phase II part. This was an exploratory group for a type of cancer without effective treatment options. Exclusion criteria was updated to exclude subjects with electrolyte abnormalities > CTCAE grade 2 and a washout period of 4 weeks was required only for live vaccines and to exclude subjects who may not comply with the study for nonmedical reasons. The ECOG performance inclusion criterion was changed to ≤ 1. The inclusion criteria of the Phase II part of the study required that the status was known for EGFR (and ALK if EGFR mutation-negative) for subjects with NSCLC, and for BRAF V600 for subjects with melanoma; included the determination of molecular parameters (EGFR, ALK, or BRAF V600 mutational status) at molecular pre-screening by a local laboratory, or by a Novartis-designated laboratory if a local laboratory test was not feasible, for subjects with a tumor of unknown status. Prohibited concomitant therapy section was updated to allow localized radiotherapy for non-target lesions
30 September 2016	Increased the duration of contraception and safety follow-up periods post spartalizumab treatment from 90 days to 150 days, using five times the upper limit of the half-life of 23 days and an added safety margin. These changes were related to an Urgent Safety Measure communicated on 08-Jun-2016 to all Investigators. With the available PK data obtained from this study an exploratory population PK (PopPK) analysis showed that the T1/2 of spartalizumab in man is 20 [17, 23] days (mean [90% CI]). Many subjects were most likely start a new antineoplastic therapy during the 150 day safety follow-up. Therefore, after the start of a new antineoplastic therapy during the safety follow-up, only AEs and SAEs suspected to be related to spartalizumab were collected in order to focus on the collection of information relevant to spartalizumab; and concomitant medications were recorded until the 30-day safety follow-up or the start of new antineoplastic, whatever occurred first. This amendment also includes new blood samples for PK and PD assays to assess RO in blood and pathway modulation in peripheral blood by analysis of circulating humoral factors and cell based markers (e.g. RNA profiling and FACS analysis of PBMC). RO samples were collected at Day1 of Cycles 1, 3 and 6 and at EoT. In addition RO and PK samples were collected 150 days after last dose. RO samples were collected from all subjects. For pharmacodynamics plasma and PBMCs were collected at Cycle 1 Day 1, Cycle 1 Day15, Cycle 3 Day 1 and 150 days after last dose.

27 July 2017	Removed the requirement for progression on prior therapy for subjects with ATC; subjects were no longer required to have received therapy prior to being eligible for treatment with spartalizumab. Outcomes for subjects with this disease are dismal with a median life expectancy after diagnosis of less than six months. Given the poor outcome after standard therapy current NCCN treatment guidelines recommend that all subjects be considered for clinical studies. The inclusion criteria was revised in this amendment to allow treatment earlier in the disease course. Specific changes to inclusion criterion #4 for subjects with ATC included: - Subjects were not required to have received or progressed on a prior therapy. - Subjects must not be at short term risk for life threatening complications (such as airway compromise or bleeding from locoregional or metastatic disease). - Chemoradiation and/or surgery was to be considered prior to study entry for those subjects with locally advanced Mutations affecting BRAF occur in approximately 11% - 27% of subjects with ATC. To facilitate a more complete understanding of the subject population benefiting from treatment with spartalizumab, tumor samples were to be tested to determine BRAF V600 mutational status. Knowledge of the BRAF mutation status was not required for study entry. ECG collection was needed only at Screening and as clinically indicated. Prohibited concomitant therapy was modified to better align with medical practice in immuno-oncology. Prohibited concomitant therapy was modified to better align with medical practice in immuno-oncology. Separate primary analyses and indication-specific complete clinical study reports could be provided for this study. Therefore, the protocol was amended to allow separate primary analyses.
16 July 2018	Incorporated health authority-requested language requiring study treatment discontinuation in the event of Stevens Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN). Revised to align with recently published guidelines on the clinical management of suspected immune-related toxicities. Removed the use of condom for male study participants receiving spartalizumab. Receptor occupancy and pharmacodynamic (PBMCs and cytokines) samples for markers were no longer to be collected post first primary CSR data cut-off. Language was updated for irRC assessment to clarify criteria for new measurable lesions and irRC response in case of only non-measurable disease at baseline. Removed the reporting of total dose per cycle from statistical section. More details and clarifications were added for reporting other secondary efficacy objectives. Modifications were made to follow Novartis analysis standards safety.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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

Notes: