Clinical trial results:
A randomized, double-blind, placebo-controlled, phase III study comparing the combination of PDR001, dabrafenib and trametinib versus placebo, dabrafenib and trametinib in previously untreated patients with unresectable or metastatic BRAF V600 mutant melanoma

Summary

EudraCT number	2016-002794-35
Trial protocol	DE SE GB ES AT CZ PL BG GR BE PT NL DK HU IT
Global end of trial date	21 August 2024

Results information

Result version number	v1
This version publication date	27 August 2025
First version publication date	27 August 2025

Trial information

Trial identification

Sponsor protocol code	CPDR001F2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02967692
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Lichtstrasse 35, Basel, Switzerland, 4056
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 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 August 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate safety and efficacy of the combination of an anti-PD-1 antibody (PDR001), a BRAF inhibitor (dabrafenib) and a MEK inhibitor (trametinib) in patients with BRAF V600 mutant, unresectable and metastatic melanoma.

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	17 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 9
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Chile: 18
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 92
Country: Number of subjects enrolled	Germany: 66
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 83
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Mexico: 3

Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Russian Federation: 51
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	Switzerland: 13
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	568
EEA total number of subjects	376

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)	409
From 65 to 84 years	157
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Part 1 and 2 were conducted in 18 centers across 12 countries. Part 3 is conducted in 190 centers across 29 countries

Pre-assignment

Screening details:

The screening phase began once written informed consent was provided and ended after 28 days or when subject received the first dose (Part 1 and 2) or was randomized (Part 3), whichever came first.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD

Arm description:

In Part 1, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).

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

Dosage and administration details:

Spartalizumab powder for solution is used in Part 1 and Part 2, and as concentrate for solution for infusion for Part 3. Spartalizumab is administered via intravenous infusion over 30 minutes once every 4 weeks

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

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

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

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

Arm title	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD

Arm description:

In Part 2, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the

approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).

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

Dosage and administration details:

Spartalizumab powder for solution is used in Part 1 and Part 2, and as concentrate for solution for infusion for Part 3. Spartalizumab is administered via intravenous infusion over 30 minutes once every 4 weeks

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

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

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

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

Arm title	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD

Arm description:

In Part 3, participants are randomized to receive Spartalizumab (PDR001) at the RP3R identified in Part 1 (400 mg Q4W) in combination with approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)

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

Dosage and administration details:

Spartalizumab powder for solution is used in Part 1 and Part 2, and as concentrate for solution for infusion for Part 3. Spartalizumab is administered via intravenous infusion over 30 minutes once every 4 weeks

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

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule

Routes of administration	Oral use

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

Arm title	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD

Arm description:

In Part 3, participants are randomized to receive matching placebo in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)

Arm type	Placebo
Investigational medicinal product name	Dabrafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

Investigational medicinal product name	Spartalizumab matching placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Powder for solution for infusion, Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab matching placebo is used as concentrate for solution for infusion for Part 3.
Spartalizumab matching placebo is administered via intravenous infusion over 30 minutes once every 4 weeks

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

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

Number of subjects in period 1	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD
Started	9	27	267
Treated	9	27	267
Completed	0	0	0
Not completed	9	27	267
Adverse event, serious fatal	-	1	13
Physician decision	-	-	22
Adverse event, non-fatal	2	9	60
Protocol deviation	1	-	1

Study terminated by sponsor	2	1	42
Progressive disease	3	15	114
Lost to follow-up	-	-	1
Subject/guardian decision	1	1	14

Number of subjects in period 1	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Started	265
Treated	264
Completed	0
Not completed	265
Adverse event, serious fatal	13
Physician decision	13
Adverse event, non-fatal	28
Protocol deviation	1
Study terminated by sponsor	37
Progressive disease	151
Lost to follow-up	-
Subject/guardian decision	22

Baseline characteristics

Reporting groups	
Reporting group title	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD
Reporting group description:	
In Part 1, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).	
Reporting group title	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD
Reporting group description:	
In Part 2, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).	
Reporting group title	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD
Reporting group description:	
In Part 3, participants are randomized to receive Spartalizumab (PDR001) at the RP3R identified in Part 1 (400 mg Q4W) in combination with approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)	
Reporting group title	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Reporting group description:	
In Part 3, participants are randomized to receive matching placebo in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)	

Reporting group values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD
Number of subjects	9	27	267
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	7	18	189
>=65 years	2	9	78
Sex: Female, Male Units: Participants			
Female	2	12	119
Male	7	15	148
Race/Ethnicity, Customized Units: Subjects			
White	9	24	225
Asian	0	2	5
Other	0	1	15
Unknown	0	0	22

Reporting group values	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD	Total	
Number of subjects	265	568	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	195	409	

>=65 years	70	159	

Sex: Female, Male Units: Participants			
Female	106	239	
Male	159	329	
Race/Ethnicity, Customized Units: Subjects			
White	227	485	
Asian	5	12	
Other	14	30	
Unknown	19	41	

End points

End points reporting groups

Reporting group title	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD

Reporting group description:

In Part 1, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).

Reporting group title	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD

Reporting group description:

In Part 2, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).

Reporting group title	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD

Reporting group description:

In Part 3, participants are randomized to receive Spartalizumab (PDR001) at the RP3R identified in Part 1 (400 mg Q4W) in combination with approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)

Reporting group title	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD

Reporting group description:

In Part 3, participants are randomized to receive matching placebo in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)

Primary: Safety Run-In (Part 1): Number of participants with dose limiting toxicities (DLTs)

End point title	Safety Run-In (Part 1): Number of participants with dose limiting toxicities (DLTs)[1][2]

End point description:

DLT was defined as an adverse event or abnormal laboratory value that was unrelated to disease, disease progression, inter-current illness, or concomitant medications and occured within 8 weeks of treatment with spartalizumab in combination with dabrafenib and trametinib. The DLT criteria included Grade 4 hematological adverse events, Grade 4 bilirubin elevation, specific gastrointestinal adverse events, symptomatic serum amylase or lipase elevation, Grade 3 or higher hypertension, Grade 3 or higher cardiac events, Grade 2 or higher pneumonitis, Grade 3 or higher immune-related toxicities, infusion-related reactions, other clinically significant adverse events, and toxicities leading to a dosing delay of over 12 weeks. NCI CTCAE v4.03 was used for grading DLTs

End point type	Primary

End point timeframe:

Up to 8 weeks (Part 1)

Notes:

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

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only applicable to Part 1 Arm

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Biomarker cohort (Part 2): Change from baseline in programmed cell death-ligand 1 (PD-L1) expression upon treatment with spartalizumab in combination with dabrafenib and trametinib

End point title	Biomarker cohort (Part 2): Change from baseline in programmed cell death-ligand 1 (PD-L1) expression upon treatment with spartalizumab in combination with dabrafenib and trametinib[3][4]

End point description:

Change from baseline in PD-L1 expression (as determined by immunohistochemistry in tissue samples) upon treatment with spartalizumab in combination with dabrafenib and trametinib in participants from Part 2

End point type	Primary

End point timeframe:

Baseline, Cycle 1 Day 15 and Cycle 3 Day 1 (Part 2). Each cycle is 28 days

Notes:

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

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only applicable to Part 2 Arm

End point values	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Percentage of positive tumor cells				
arithmetic mean (standard deviation)				
Cycle 1 Day 15	1.7 (± 13.05)			
Cycle 3 Day 1	2.7 (± 7.63)			

Statistical analyses

No statistical analyses for this end point

Primary: Biomarker cohort (Part 2): Change from baseline in CD8+ cells upon treatment with spartalizumab in combination with dabrafenib and trametinib

End point title	Biomarker cohort (Part 2): Change from baseline in CD8+ cells upon treatment with spartalizumab in combination with dabrafenib and trametinib[5][6]

End point description:

Change from baseline in CD8+ cells (as determined by flow cytometry in blood samples) upon treatment with spartalizumab in combination with dabrafenib and trametinib in participants from Part 2

End point type	Primary

End point timeframe:

Baseline, Cycle 1 Day 15 and Cycle 3 Day 1 (Part 2). Each cycle is 28 days

Notes:

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

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only applicable to Part 2 Arm

End point values	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage Marker Area				
arithmetic mean (standard deviation)				
Cycle 1 Day 15	0.4 (± 3.22)			
Cycle 3 Day 1	1.2 (± 2.43)			

Statistical analyses

No statistical analyses for this end point

Primary: Randomized (Part 3): Progression-Free Survival (PFS) as per investigator's assessment by RECIST 1.1

End point title	Randomized (Part 3): Progression-Free Survival (PFS) as per investigator's assessment by RECIST 1.1[7]

End point description:

Progression-free survival was defined as the time from the date of first dose to the date of the first documented radiological progression per investigator's assessment according to RECIST 1.1 or death due to any cause. The distribution of PFS was estimated using the Kaplan-Meier (KM) method. If a patient had not had an event at the time of data cut-off, progression-free survival was censored at the date of last adequate tumor assessment.

End point type	Primary

End point timeframe:

Up to disease progression or death due to any cause, whichever occurs first, assessed up to 2.8 years (Part 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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	265		
Units: Months				
median (confidence interval 95%)	16.2 (12.7 to 23.9)	12.0 (10.2 to 15.4)		

Statistical analyses

Statistical analysis title	P3: PFS per inv. assessment (RECIST 1.1)
Comparison groups	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD v P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Number of subjects included in analysis	532
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.042
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	Other: 2 %
sides	2-sided
lower limit	0.655
upper limit	1.027

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description:	
Overall survival was defined as the time from date of randomization to date of death due to any cause	
End point type	Secondary
End point timeframe:	
Up to death due to any cause, assessed up to approximately 7 years	

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	27	267	265
Units: Months				
median (confidence interval 95%)	999 (12.2 to 999)	30.7 (21.3 to 67.4)	61.5 (41.6 to 999)	41.6 (30.6 to 56.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR) as per investigator's assessment by RECIST 1.1

End point title	Overall response rate (ORR) as per investigator's assessment by RECIST 1.1

End point description:

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

End point type	Secondary

End point timeframe:

Part 1: Up to 3.3 years. Part 2: Up to 3 years. Part 3: Up to 2.8 years

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	27	267	265
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (66.4 to 100.0)	70.4 (49.8 to 86.2)	68.5 (62.6 to 74.1)	64.2 (58.1 to 69.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) as per investigator’s assessment by RECIST 1.1

End point title	Duration of response (DOR) as per investigator’s assessment by RECIST 1.1

End point description:

DOR was defined as the time from first documented response of CR or PR to date of first documented progression or death, according to RECIST 1.1 criteria. The distribution of DOR was estimated using the KM method. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters

End point type	Secondary

End point timeframe:

From first documented response to date of first documented progression or death, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3)

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	19	183	170
Units: Months				
median (confidence interval 95%)	999 (8.3 to 999)	20.0 (9.4 to 999)	999 (18.6 to 999)	20.7 (13.0 to 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR) as per investigator’s assessment by RECIST 1.1

End point title	Disease control rate (DCR) as per investigator’s assessment by RECIST 1.1

End point description:

DCR was defined as the percentage of participants with CR or PR or subjects with stable disease (SD) lasting for a duration of at least 24 weeks as per local review according to RECIST 1.1 criteria. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary

End point timeframe:

Part 1: Up to 3.3 years. Part 2: Up to 3 years. Part 3: Up to 2.8 year

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	27	267	265
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (66.4 to 100.0)	92.6 (75.7 to 99.1)	84.3 (79.3 to 88.4)	86.4 (81.7 to 90.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global health status scores

End point title	Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global health status scores[8]

End point description:

The EORTC QLQ-C30 was a 30-item questionnaire that patients complete, consisting of both multi-item scales and single-item measures. It included five functional scales, three symptom scales, six single items, and a Global Health Status/Quality of Life (GHS/QoL) scale. The GHS/QoL scale had seven possible response scores ranging from 1 (very poor) to 7 (excellent), which were averaged and transformed to a 0-100 scale. A higher score on this scale indicated a better quality of life. The change from baseline in GHS/QoL scores was calculated. A positive change from baseline indicated improvement in the patient's quality of life.

End point type	Secondary

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	186		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Cycle 4 Day 1	0.81 (± 19.300)	2.20 (± 24.918)		
Cycle 6 Day 1	1.22 (± 25.050)	1.90 (± 21.197)		
Cycle 8 Day 1	0.00 (± 24.526)	0.50 (± 19.608)		
Cycle 10 Day 1	1.88 (± 23.088)	0.27 (± 18.752)		
Cycle 12 Day 1	0.61 (± 25.906)	0.00 (± 24.541)		
Cycle 14 Day 1	0.65 (± 23.561)	-0.89 (± 23.306)		
Cycle 16 Day 1	0.82 (± 25.186)	1.76 (± 24.142)		
Cycle 18 Day 1	-0.46 (± 24.106)	-0.10 (± 19.193)		
Cycle 20 Day 1	1.93 (± 21.766)	-1.02 (± 23.144)		
Cycle 22 Day 1	0.95 (± 22.047)	2.29 (± 21.947)		
Cycle 25 Day 1	3.57 (± 23.981)	-0.24 (± 25.497)		
Cycle 28 Day 1	4.50 (± 19.793)	1.06 (± 22.513)		
Cycle 31 Day 1	11.59 (± 24.967)	6.73 (± 21.084)		

Cycle 34 Day 1	16.67 (± 47.140)	13.89 (± 20.184)		
30 days post-progression	-11.59 (± 24.967)	-7.78 (± 29.274)		
60 days post-progression	-11.54 (± 16.506)	-17.19 (± 24.050)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Physical functioning scale scores

End point title	Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Physical functioning scale scores[9]

End point description:

The EORTC QLQ-C30 was a patient completed 30 item questionnaire that was composed of both multi-item scales and single-item measures. These included five functional scales, three symptom scales, six single items and a global health status/QoL scale. The EORTC QLQ-C30 physical functioning scale measured a patient's ability to carry out daily activities and tasks requiring physical exertion. It consisted of five questions asking patients to rate their level of physical functioning, with response options ranging from 1="not at all" to 4="very much". The scores for each item were summed and transformed to a 0 to 100 scale, with higher scores indicating better physical functioning. The change from baseline in physical functioning scale scores was calculated. A positive change from baseline indicated improvement in physical functioning.

End point type	Secondary

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	186		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Cycle 4 Day 1	-1.52 (± 16.243)	-0.70 (± 17.618)		
Cycle 6 Day 1	-2.38 (± 16.121)	-0.60 (± 14.824)		
Cycle 8 Day 1	-1.29 (± 18.350)	-0.59 (± 15.687)		
Cycle 10 Day 1	-0.18 (± 17.985)	-1.11 (± 13.736)		
Cycle 12 Day 1	-1.39 (± 18.108)	-0.85 (± 10.652)		
Cycle 14 Day 1	-2.42 (± 16.720)	-2.61 (± 12.320)		

Cycle 16 Day 1	-4.19 (± 20.301)	-2.24 (± 13.331)		
Cycle 18 Day 1	-3.48 (± 18.862)	-3.55 (± 13.474)		
Cycle 20 Day 1	-4.07 (± 15.316)	-1.73 (± 11.536)		
Cycle 22 Day 1	-3.21 (± 15.538)	-0.85 (± 11.157)		
Cycle 25 Day 1	-1.35 (± 16.510)	-2.67 (± 13.158)		
Cycle 28 Day 1	-0.80 (± 13.843)	-2.67 (± 15.953)		
Cycle 31 Day 1	-2.03 (± 10.719)	-1.79 (± 9.533)		
Cycle 34 Day 1	0.00 (± 0.000)	-3.33 (± 5.578)		
30 days post-progression	-6.67 (± 18.641)	-8.67 (± 19.973)		
60 days post-progression	-13.85 (± 15.977)	-21.25 (± 27.991)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Pain symptom scale scores

End point title	Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Pain symptom scale scores[10]

End point description:

The EORTC QLQ-C30 was a patient completed 30 item questionnaire that was composed of both multi-item scales and single-item measures. These included five functional scales, three symptom scales, six single items and a global health status/QoL scale. The EORTC QLQ-C30 pain symptom scale was one of the symptom scales in the questionnaire, which measured the severity of pain experienced by the patient. The pain symptom scale consisted of two items, one measuring the severity of pain and the other measuring the use of painkillers. The items were rated on a 4-point scale ranging from 1="not at all" to 4="very much". The scores for each item were summed and transformed to a 0 to 100 scale, with higher scores indicating more severe pain. The change from baseline in pain symptom scale scores was calculated. A negative change from baseline indicated improvement.

End point type	Secondary

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	186		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Cycle 4 Day 1	-5.24 (± 26.434)	-5.29 (± 24.881)		
Cycle 6 Day 1	-6.43 (± 28.820)	-7.49 (± 23.611)		
Cycle 8 Day 1	-4.91 (± 29.176)	-4.11 (± 24.420)		
Cycle 10 Day 1	-7.95 (± 28.346)	-4.76 (± 23.557)		
Cycle 12 Day 1	-8.33 (± 28.890)	-5.26 (± 22.646)		
Cycle 14 Day 1	-5.50 (± 28.140)	-3.56 (± 23.062)		
Cycle 16 Day 1	-5.86 (± 26.220)	-4.44 (± 25.820)		
Cycle 18 Day 1	-3.15 (± 30.178)	-3.21 (± 20.898)		
Cycle 20 Day 1	-4.47 (± 30.659)	-2.85 (± 23.249)		
Cycle 22 Day 1	-5.49 (± 27.049)	-3.54 (± 23.969)		
Cycle 25 Day 1	-6.25 (± 28.868)	-4.76 (± 20.685)		
Cycle 28 Day 1	-3.00 (± 26.872)	-3.03 (± 22.701)		
Cycle 31 Day 1	-10.14 (± 24.995)	-7.05 (± 34.696)		
Cycle 34 Day 1	-8.33 (± 11.785)	-5.56 (± 8.607)		
30 days post-progression	9.42 (± 28.791)	0.56 (± 28.190)		
60 days post-progression	15.38 (± 19.792)	11.46 (± 24.884)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Time to 10 point definitive deterioration in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global Health Status

End point title	Randomized (Part 3): Time to 10 point definitive deterioration in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global Health Status[11]

End point description:

The EORTC QLQ-C30 was a patient completed 30 item questionnaire that was composed of both multi-item scales and single-item measures. These included five functional scales, three symptom scales, six single items and a global health status/QoL scale. The GHS/QoL scale had seven possible response scores ranging from 1 (very poor) to 7 (excellent), which were averaged and transformed to a 0-100

scale. A higher score on this scale indicated a better quality of life. The time to definitive 10 point deterioration is defined as the time from the date of randomization to the date of event, which is defined as at least 10 points relative to baseline worsening of the GHS/QoL score or death due to any cause. If a subject had not had an event, the time to deterioration was censored at the date of the last adequate assessment. The distribution was estimated using KM method.

End point type	Secondary

End point timeframe:

From baseline to date of at least 10 points relative to baseline worsening of the global health status score or death due to any cause, up to 2.8 years (Part 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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	265		
Units: Months				
median (confidence interval 95%)	19.4 (15.7 to 24.9)	22.1 (17.5 to 999)		

Statistical analyses

Statistical analysis title	P3: Time to 10pt def. det. in EORTC QLQ-C30 GHS
Comparison groups	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD v P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Number of subjects included in analysis	532
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2975
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.183
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.865
upper limit	1.619

Secondary: Randomized (Part 3): Change from baseline in Function Assessment Cancer Therapy-melanoma (FACT-M) melanoma subscale score

End point title	Randomized (Part 3): Change from baseline in Function Assessment Cancer Therapy-melanoma (FACT-M) melanoma subscale score[12]

End point description:

The Functional Assessment of Cancer Therapy–Melanoma (FACT-M) quality of life questionnaire was composed of the FACT-General (FACT-G) plus the Melanoma Subscale and the Melanoma Surgery

Subscale, which complemented the general scale with items specific to quality of life (QoL) in melanoma. The Melanoma Subscale of FACT-M included 16 questions, with response options of 0= "Not at all", 1= "a little bit", 2= "somewhat", 3= "quite a bit" and 4= "very much". The FACT-M melanoma subscale score ranged from 0 to 64, with higher scores indicating a higher quality of life in relation to melanoma. The change from baseline in melanoma subscale scores was calculated. A positive change from baseline indicated improvement.

End point type	Secondary

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	190		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 4 Day 1	0.83 (± 6.600)	0.87 (± 6.185)		
Cycle 6 Day 1	1.01 (± 7.370)	1.18 (± 6.219)		
Cycle 8 Day 1	1.14 (± 7.284)	1.09 (± 5.742)		
Cycle 10 Day 1	1.52 (± 7.314)	0.54 (± 6.492)		
Cycle 12 Day 1	1.21 (± 7.515)	0.47 (± 5.974)		
Cycle 14 Day 1	0.77 (± 7.071)	0.65 (± 6.681)		
Cycle 16 Day 1	0.93 (± 6.451)	0.71 (± 6.374)		
Cycle 18 Day 1	1.23 (± 7.095)	0.47 (± 6.152)		
Cycle 20 Day 1	1.28 (± 6.634)	0.53 (± 5.875)		
Cycle 22 Day 1	1.87 (± 6.215)	0.79 (± 5.970)		
Cycle 25 Day 1	2.73 (± 5.950)	0.74 (± 6.792)		
Cycle 28 Day 1	2.46 (± 5.195)	0.61 (± 8.020)		
Cycle 31 Day 1	3.29 (± 5.702)	1.88 (± 6.154)		
Cycle 34 Day 1	-0.50 (± 2.121)	4.60 (± 3.578)		
30 days post-progression	0.33 (± 7.620)	-1.07 (± 8.590)		
60 days post-progression	-2.60 (± 5.734)	-3.06 (± 8.948)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in EuroQoL 5-level instrument (EQ-5D-5L)- Visual Analog Scale (VAS) score

End point title	Randomized (Part 3): Change from baseline in EuroQoL 5-level instrument (EQ-5D-5L)- Visual Analog Scale (VAS) score[13]

End point description:

The EQ-5D-5L is a standardized questionnaire used to assess health-related quality of life, and it

includes a Visual Analog Scale (VAS). The VAS score is obtained by asking the individual to rate their current health status on a scale from 0 to 100, where 0 represents the worst possible health state and 100 represents the best possible health state. The change from baseline in EQ-5D-5L VAS score was calculated. A positive change from baseline indicates improvement in the health status.

End point type	Secondary

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 3)

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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	176	190		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Cycle 4 Day 1	1.85 (± 16.567)	2.16 (± 19.733)		
Cycle 6 Day 1	1.55 (± 20.751)	3.10 (± 16.095)		
Cycle 8 Day 1	0.39 (± 20.246)	2.60 (± 15.200)		
Cycle 10 Day 1	2.45 (± 19.050)	2.52 (± 16.144)		
Cycle 12 Day 1	1.88 (± 24.653)	1.42 (± 15.695)		
Cycle 14 Day 1	2.62 (± 19.455)	1.71 (± 14.337)		
Cycle 16 Day 1	1.30 (± 18.640)	2.79 (± 16.996)		
Cycle 18 Day 1	2.16 (± 20.762)	1.91 (± 16.743)		
Cycle 20 Day 1	1.34 (± 17.831)	1.28 (± 16.108)		
Cycle 22 Day 1	3.01 (± 19.102)	1.55 (± 14.973)		
Cycle 25 Day 1	4.47 (± 19.489)	0.26 (± 14.784)		
Cycle 28 Day 1	4.20 (± 17.545)	-0.39 (± 18.529)		
Cycle 31 Day 1	6.45 (± 19.561)	-0.08 (± 16.747)		
Cycle 34 Day 1	-9.50 (± 14.849)	5.60 (± 19.008)		
30 days post-progression	-4.04 (± 22.033)	-10.24 (± 23.532)		
60 days post-progression	-19.25 (± 19.923)	-8.19 (± 21.192)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): PFS as per investigator's assessment by RECIST 1.1 by PD-L1 expression

End point title	Randomized (Part 3): PFS as per investigator's assessment by RECIST 1.1 by PD-L1 expression[14]

End point description:

PFS was defined as the time from the date of first dose to the date of the first documented radiological progression as per investigator's assessment using RECIST 1.1 response criteria or death due to any cause. The distribution of PFS was estimated using the KM method. If a patient had not had an event at the time of data cut-off, progression-free survival was censored at the date of last adequate tumor assessment. PFS analysis was performed by PD-L1 status (positive, negative) where a positive status was defined as having ≥ 1% expression and a negative status was defined as having < 1% expression.

End point type	Secondary

End point timeframe:

Up to disease progression or death due to any cause, up to 2.8 years (Part 3)

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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	241		
Units: Months				
median (confidence interval 95%)				
PD-L1 negative (<1%)	12.0 (10.1 to 15.7)	10.3 (7.5 to 13.0)		
PD-L1 positive (>=1%)	26.6 (17.4 to 999)	15.4 (10.2 to 25.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): OS by PD-L1 expression

End point title	Randomized (Part 3): OS by PD-L1 expression[15]

End point description:

Overall survival was defined as the time from date of randomization to date of death due to any cause. OS analysis was performed by PD-L1 subgroup (positive, negative) where a positive status was defined as having ≥ 1% expression and a negative status was defined as having < 1% expression.

End point type	Secondary

End point timeframe:

Up to death due to any cause, assessed up to approximately 7 years

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: Only applicable to Part 3-Arm 1 and Part 3-Arm 2

End point values	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	138		
Units: Months				
median (confidence interval 95%)				
PD-L1 negative (<1%)	41.6 (27.6 to 999)	21.0 (16.9 to 33.4)		
PD-L1 positive (>=1%)	999 (45.4 to 999)	61.3 (41.2 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Spartalizumab ADA incidence

End point title	Spartalizumab ADA incidence[16]

End point description:

Spartalizumab ADA incidence was calculated as the percentage of participants who were treatment-induced spartalizumab ADA positive (post-baseline ADA positive with ADA-negative sample at baseline) and treatment-boosted spartalizumab ADA positive (post-baseline ADA positive with titer that is at least the fold titer change greater than the ADA-positive baseline titer)

End point type	Secondary

End point timeframe:

Throughout study until 150 days after the last dose of spartalizumab, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3).

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: Only applicable to Part 1, Part 2 and Part 3-Arm 1

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	26	244	
Units: Participants	0	5	55	

Statistical analyses

No statistical analyses for this end point

Secondary: Spartalizumab Anti-drug Antibody (ADA) prevalence at baseline

End point title	Spartalizumab Anti-drug Antibody (ADA) prevalence at

End point description:

Spartalizumab ADA prevalence at baseline was calculated as the percentage of participants who had an spartalizumab ADA positive result at baseline.

End point type	Secondary

End point timeframe:

Baseline

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: Only applicable to Part 1, Part 2 and Part 3-Arm 1

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	26	244	
Units: Participants	0	0	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration (Ctrough) for spartalizumab

End point title	Trough concentration (Ctrough) for spartalizumab[18]

End point description:

Ctrough for spartalizumab refers to the serum concentration of spartalizumab immediately prior to the administration of a dose of spartalizumab on Day 1 of Cycle 2 and later cycles.

End point type	Secondary

End point timeframe:

Pre-infusion on Day 1 of each Cycle starting from Cycle 2, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). Cycle=28 days

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: Only applicable to Part 1, Part 2 and Part 3-Arm 1

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	17	138	
Units: microgram (µg)/miliLiter (mL)				
arithmetic mean (standard deviation)				
Cycle 2	31.9 (± 4.59)	31.5 (± 20.3)	28.4 (± 13.4)	
Cycle 3	41.1 (± 7.07)	56.1 (± 34.2)	43.5 (± 19.1)	
Cycle 4	47.8 (± 999)	46.9 (± 18.8)	50.5 (± 24.2)	
Cycle 5	46.3 (± 999)	56.7 (± 19.5)	56.4 (± 24.5)	
Cycle 6	53.8 (± 16.9)	60.9 (± 23.6)	58.8 (± 26.5)	

Cycle 7	56.1 (± 12.1)	62.2 (± 33.3)	63.7 (± 29.6)	
Cycle 8	57.9 (± 12.7)	65.8 (± 32.8)	64.1 (± 29.9)	
Cycle 9	60.2 (± 30.9)	69.5 (± 25.2)	67.8 (± 33.5)	
Cycle 10	62.1 (± 22.5)	68.4 (± 33.2)	63.8 (± 28.4)	
Cycle 11	66.9 (± 15.8)	63.2 (± 35.8)	62.1 (± 27.9)	
Cycle 12	67.0 (± 16.5)	61.6 (± 29.3)	60.7 (± 27.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose plasma concentration for dabrafenib

End point title	Pre-dose plasma concentration for dabrafenib

End point description:

Plasma concentration of dabrafenib immediately prior to the administration of a dose of dabrafenib.

End point type	Secondary

End point timeframe:

Pre-infusion on Day 1 of every cycle from Cycle 2 to 12, and then every 6 cycles from Cycle 18 to 36, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). Cycle=28 days

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	18	127	162
Units: nanogram (ng)/ miliLiter (mL)				
arithmetic mean (standard deviation)				
Cycle 2	33.7 (± 27.4)	149 (± 391)	208 (± 473)	234 (± 475)
Cycle 3	25.5 (± 10.4)	183 (± 469)	192 (± 607)	135 (± 266)
Cycle 4	23.0 (± 15.8)	372 (± 811)	169 (± 404)	167 (± 328)
Cycle 5	28.8 (± 30.6)	152 (± 293)	130 (± 317)	152 (± 363)
Cycle 6	15.1 (± 16.3)	73.7 (± 131)	198 (± 521)	94.6 (± 186)
Cycle 7	20.9 (± 13.9)	40.0 (± 20.0)	180 (± 510)	121 (± 279)
Cycle 8	22.9 (± 16.8)	28.0 (± 10.4)	173 (± 532)	97.2 (± 177)
Cycle 9	22.3 (± 7.59)	43.3 (± 40.6)	143 (± 394)	133 (± 259)
Cycle 10	24.5 (± 9.19)	60.0 (± 28.3)	167 (± 472)	122 (± 266)
Cycle 11	154 (± 250)	33.8 (± 22.6)	174 (± 667)	119 (± 238)
Cycle 12	10.9 (± 10.3)	41.3 (± 37.2)	148 (± 396)	146 (± 295)
Cycle 18	19.0 (± 999)	50.6 (± 49.7)	180 (± 618)	167 (± 385)
Cycle 24	999 (± 999)	91.5 (± 98.3)	147 (± 344)	60.2 (± 67.9)
Cycle 30	40.2 (± 999)	999 (± 999)	226 (± 488)	47.6 (± 23.2)
Cycle 36	47.6 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose plasma concentration for trametinib

End point title	Pre-dose plasma concentration for trametinib

End point description:

Plasma concentration of trametinib immediately prior to the administration of a dose of trametinib.

End point type	Secondary

End point timeframe:

Pre-infusion on Day 1 of every cycle from Cycle 2 to 12, and then every 6 cycles from Cycle 18 to 36, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). Cycle=28 days

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	14	103	143
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 2	11.7 (± 4.09)	11.2 (± 3.4)	11.5 (± 4.73)	13.9 (± 9.36)
Cycle 3	8.34 (± 0.354)	12.2 (± 2.55)	11.4 (± 5.98)	12.3 (± 5.59)
Cycle 4	10.7 (± 1.64)	12.5 (± 4.84)	11.7 (± 4.62)	11.9 (± 5.04)
Cycle 5	10.1 (± 999)	12.6 (± 5.03)	11.3 (± 4.91)	11.6 (± 4.49)
Cycle 6	10.0 (± 1.38)	11.8 (± 3.73)	11.6 (± 5.12)	10.9 (± 3.52)
Cycle 7	11.6 (± 3.8)	11.8 (± 5.24)	12.0 (± 4.86)	11.0 (± 4.26)
Cycle 8	9.24 (± 3.06)	10.2 (± 4.13)	10.3 (± 3.92)	11.3 (± 4.08)
Cycle 9	8.73 (± 3.35)	10.5 (± 4.43)	10.9 (± 4.57)	11.6 (± 4.22)
Cycle 10	8.24 (± 999)	10.5 (± 4.02)	10.9 (± 4.47)	11.8 (± 4.26)
Cycle 11	10.7 (± 999)	11.6 (± 4.69)	10.3 (± 3.67)	11.4 (± 3.57)
Cycle 12	10.6 (± 3.92)	11.0 (± 4.53)	10.6 (± 4.31)	11.2 (± 3.82)
Cycle 18	10.1 (± 999)	13.0 (± 4.6)	9.66 (± 3.49)	12.1 (± 5.13)
Cycle 24	999 (± 999)	13.4 (± 8.03)	10.7 (± 4.89)	10.7 (± 2.21)
Cycle 30	10.8 (± 999)	999 (± 999)	9.34 (± 7.56)	10.1 (± 2.76)
Cycle 36	8.97 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose interruptions

End point title	Number of participants with dose interruptions

End point description:

Number of participants with dose interruptions for spartalizumab, dabrafenib and trametinib

End point type	Secondary

End point timeframe:

From baseline to end of treatment, assessed up to approximately 7 years

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	27	267	264
Units: Participants				
Spartalizumab|With no dose interruption	4	11	120	170
Dabrafenib|With no dose interruption	0	2	29	74
Trametinib|With no dose interruption	0	1	29	64
Spartalizumab|With at least one dose interruption	5	16	147	94
Dabrafenib|With at least one dose interruption	9	25	238	190
Trametinib|With at least one dose interruption	9	26	238	200

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose reductions

End point title	Number of participants with dose reductions

End point description:

Number of patients with dose reductions for spartalizumab, dabrafenib and trametinib

End point type	Secondary

End point timeframe:

From baseline to end of treatment, assessed up to approximately 7 years

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	27	267	264
Units: Participants				
Dabrafenib|No dose reduction or interruption	0	2	25	68
Trametinib|No dose reduction or interruption	0	1	28	63
Dabrafenib|≥1 dose red./interruption	9	25	242	196
Trametinib|≥1 dose red./interruption	9	26	239	201

Statistical analyses

No statistical analyses for this end point

Secondary: Relative dose intensity

End point title	Relative dose intensity

End point description:

Relative dose intensity for spartalizumab, dabrafenib and trametinib computed as the ratio (expressed as percentage) of dose intensity and planned dose intensity:
* Spartalizumab (PDR001) = [Dose intensity (mg/4W) / planned dose intensity (mg/4W)]*100.
* Trametinib and Dabrafenib = [Dose intensity (mg/day) / planned dose intensity (mg/day)]*100.

End point type	Secondary

End point timeframe:

From baseline to end of treatment, assessed up to approximately 7 years

End point values	P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD	P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	27	267	264
Units: Percentage of planned dose intensity				
arithmetic mean (standard deviation)				
Spartalizumab (PDR001)	90.7 (± 16.83)	91.7 (± 10.41)	94.4 (± 9.21)	97.5 (± 5.33)
Dabrafenib	62.2 (± 26.36)	71.3 (± 21.13)	78.1 (± 21.21)	89.6 (± 15.10)
Trametinib	65.9 (± 16.90)	76.2 (± 17.19)	79.8 (± 19.58)	89.5 (± 14.86)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events (AEs) were collected from first dose of study medication until the last dose plus 30 days safety follow-up, assessed up to approximately 86 months.	
Adverse event reporting additional description:	
Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Part I PDR001 + D + T
Reporting group description:	
Part I PDR001 + D + T	
Reporting group title	Part III Placebo + D + T
Reporting group description:	
Part III Placebo + D + T	
Reporting group title	Part III PDR001 + D + T
Reporting group description:	
Part III PDR001 + D + T	
Reporting group title	Part II PDR001 + D + T
Reporting group description:	
Part II PDR001 + D + T	

Serious adverse events	Part I PDR001 + D + T	Part III Placebo + D + T	Part III PDR001 + D + T
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)	123 / 264 (46.59%)	151 / 267 (56.55%)
number of deaths (all causes)	2	33	28
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to meninges			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Malignant melanoma in situ			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign breast neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	2 / 3	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm malignant			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
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-Hodgkin's lymphoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oncologic complication			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			

subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Uterine neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aneurysm ruptured			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Embolism			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Vasculitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Lymphoedema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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 arterial occlusive disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General disorders and administration site conditions			
Administration site extravasation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	4 / 267 (1.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	1 / 3	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	4 / 9 (44.44%)	16 / 264 (6.06%)	46 / 267 (17.23%)
occurrences causally related to treatment / all	7 / 7	22 / 25	65 / 70
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Sarcoidosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytokine release syndrome			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Prostatic disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Autoimmune lung disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	6 / 264 (2.27%)	7 / 267 (2.62%)
occurrences causally related to treatment / all	0 / 0	2 / 6	2 / 8
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	9 / 267 (3.37%)
occurrences causally related to treatment / all	0 / 0	2 / 2	9 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory arrest			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase abnormal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (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
Aspartate aminotransferase abnormal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Amylase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	4 / 267 (1.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Body temperature increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Ejection fraction decreased			
subjects affected / exposed	1 / 9 (11.11%)	15 / 264 (5.68%)	17 / 267 (6.37%)
occurrences causally related to treatment / all	1 / 1	16 / 18	18 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcus test positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Fall			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Head injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
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 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Post embolisation syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Scapula fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Road traffic accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Rib fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Subdural haematoma			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Angina unstable			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Bradycardia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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 / 9 (0.00%)	0 / 264 (0.00%)	0 / 267 (0.00%)
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 disorder			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Left ventricular dysfunction			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
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 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Sinus tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amnesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Cerebral haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Epilepsy			

subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	0 / 267 (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
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Headache			
subjects affected / exposed	0 / 9 (0.00%)	4 / 264 (1.52%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	1 / 4	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
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	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune-mediated encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Nerve compression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Neuritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological decompensation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Partial seizures			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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 motor neuropathy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Polyneuropathy			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	2 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 9 (0.00%)	4 / 264 (1.52%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Febrile neutropenia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Cataract			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angle closure glaucoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Detachment of retinal pigment			

epithelium			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diplopia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vision blurred			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal degeneration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Macular detachment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	5 / 267 (1.87%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	5 / 267 (1.87%)
occurrences causally related to treatment / all	0 / 0	0 / 0	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphthous ulcer			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Abdominal wall haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Colitis ulcerative			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	1 / 1	1 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Inguinal hernia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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 perforation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (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 / 9 (0.00%)	5 / 264 (1.89%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	3 / 5	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	4 / 267 (1.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Hepatitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (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
Hepatotoxicity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis acneiform			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	0 / 267 (0.00%)
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			
Immune-mediated nephritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	9 / 267 (3.37%)
occurrences causally related to treatment / all	1 / 1	2 / 3	6 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			

subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	0 / 267 (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
Urinary retention			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
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			
Hypophysitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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

Back pain			
subjects affected / exposed	0 / 9 (0.00%)	4 / 264 (1.52%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Intervertebral disc disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Soft tissue necrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sacral pain			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Pathological fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial food poisoning			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
COVID-19 pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	5 / 267 (1.87%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Device related infection			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pustular			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Pyelonephritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	5 / 267 (1.87%)
occurrences causally related to treatment / all	0 / 1	0 / 3	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Post procedural sepsis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (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
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sweating fever			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	5 / 267 (1.87%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary tract infection fungal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	3 / 267 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
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 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (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	Part II PDR001 + D + T		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 27 (66.67%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to meninges			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma in situ			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign breast neoplasm			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Basal cell carcinoma				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Adenocarcinoma pancreas				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm malignant				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-Hodgkin's lymphoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oncologic complication				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroid neoplasm				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract neoplasm				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine neoplasm				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aneurysm ruptured				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vasculitis				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shock haemorrhagic				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Administration site extravasation				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza like illness				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chills				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Discomfort				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				

subjects affected / exposed	4 / 27 (14.81%)		
occurrences causally related to treatment / all	8 / 8		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sarcoidosis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytokine release syndrome			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostatic disorder			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Autoimmune lung disease			

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Delirium				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				

Alanine aminotransferase increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase abnormal				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase abnormal				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amylase increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Body temperature increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General physical condition abnormal				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ejection fraction decreased				
subjects affected / exposed	3 / 27 (11.11%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcus test positive				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Craniocerebral injury				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post embolisation syndrome				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scapula fracture				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				

subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arteriosclerosis coronary artery				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Altered state of consciousness				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amnesia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haematoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysarthria				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningism				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic cerebral infarction				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial tumour haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial pressure increased				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated encephalopathy				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Monoparesis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nerve compression				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuritis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological decompensation				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuropathy peripheral				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraesthesia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral motor neuropathy				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Polyneuropathy				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tremor				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy mediastinal				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Conjunctival haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cataract				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angle closure glaucoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Detachment of retinal pigment epithelium				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diplopia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Vision blurred			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uveitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal degeneration			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Macular detachment			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iridocyclitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Autoimmune colitis			

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aphthous ulcer				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal wall haematoma				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ischaemic				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Autoimmune hepatitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatotoxicity				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertransaminasaemia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Portal vein thrombosis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated hepatitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin ulcer				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis acneiform				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis exfoliative generalised				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Immune-mediated nephritis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephritis				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urethral stenosis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial nephritis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract obstruction				

subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adrenal insufficiency			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypothyroidism			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bursitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Intervertebral disc disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle haemorrhage				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue necrosis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sacral pain				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis perforated				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial food poisoning				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary tract infection				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash pustular				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural sepsis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sweating fever				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				

subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection fungal				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus inadequate control				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				

subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part I PDR001 + D + T	Part III Placebo + D + T	Part III PDR001 + D + T
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	250 / 264 (94.70%)	262 / 267 (98.13%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibrous histiocytoma			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	1	1	0
Basal cell carcinoma			
subjects affected / exposed	1 / 9 (11.11%)	9 / 264 (3.41%)	2 / 267 (0.75%)
occurrences (all)	4	12	4
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 9 (0.00%)	4 / 264 (1.52%)	5 / 267 (1.87%)
occurrences (all)	0	5	5
Superficial vein thrombosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	2 / 9 (22.22%)	7 / 264 (2.65%)	10 / 267 (3.75%)
occurrences (all)	3	8	11
Lymphoedema			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	7 / 267 (2.62%)
occurrences (all)	1	4	7
Orthostatic hypotension			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	0 / 267 (0.00%)
occurrences (all)	0	4	0
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	34 / 264 (12.88%)	20 / 267 (7.49%)
occurrences (all)	0	43	25
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	8 / 267 (3.00%)
occurrences (all)	1	2	9

Fatigue			
subjects affected / exposed	7 / 9 (77.78%)	69 / 264 (26.14%)	71 / 267 (26.59%)
occurrences (all)	9	141	115
Influenza like illness			
subjects affected / exposed	4 / 9 (44.44%)	15 / 264 (5.68%)	28 / 267 (10.49%)
occurrences (all)	6	21	208
Non-cardiac chest pain			
subjects affected / exposed	2 / 9 (22.22%)	1 / 264 (0.38%)	5 / 267 (1.87%)
occurrences (all)	2	1	5
Oedema			
subjects affected / exposed	0 / 9 (0.00%)	7 / 264 (2.65%)	3 / 267 (1.12%)
occurrences (all)	0	7	3
Oedema due to cardiac disease			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	8 / 9 (88.89%)	63 / 264 (23.86%)	86 / 267 (32.21%)
occurrences (all)	17	148	303
Axillary pain			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	4 / 267 (1.50%)
occurrences (all)	0	3	4
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	55 / 264 (20.83%)	73 / 267 (27.34%)
occurrences (all)	2	116	107
Oedema peripheral			
subjects affected / exposed	1 / 9 (11.11%)	28 / 264 (10.61%)	30 / 267 (11.24%)
occurrences (all)	1	29	34
Pain			
subjects affected / exposed	1 / 9 (11.11%)	10 / 264 (3.79%)	7 / 267 (2.62%)
occurrences (all)	1	14	10
Pyrexia			
subjects affected / exposed	9 / 9 (100.00%)	145 / 264 (54.92%)	189 / 267 (70.79%)
occurrences (all)	59	670	1330
Xerosis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	3 / 267 (1.12%)
occurrences (all)	0	2	4

Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Sarcoidosis			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	5 / 267 (1.87%)
occurrences (all)	1	2	5
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences (all)	1	2	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)	30 / 264 (11.36%)	37 / 267 (13.86%)
occurrences (all)	1	36	40
Cough			
subjects affected / exposed	6 / 9 (66.67%)	49 / 264 (18.56%)	63 / 267 (23.60%)
occurrences (all)	10	63	102
Epistaxis			
subjects affected / exposed	1 / 9 (11.11%)	8 / 264 (3.03%)	17 / 267 (6.37%)
occurrences (all)	2	9	31
Oropharyngeal pain			
subjects affected / exposed	2 / 9 (22.22%)	11 / 264 (4.17%)	10 / 267 (3.75%)
occurrences (all)	4	12	11
Pleurisy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	3 / 9 (33.33%)	4 / 264 (1.52%)	28 / 267 (10.49%)
occurrences (all)	3	4	38
Pulmonary embolism			
subjects affected / exposed	1 / 9 (11.11%)	6 / 264 (2.27%)	12 / 267 (4.49%)
occurrences (all)	1	6	12
Pulmonary haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0

Rhinorrhoea			
subjects affected / exposed	1 / 9 (11.11%)	5 / 264 (1.89%)	10 / 267 (3.75%)
occurrences (all)	1	5	13
Sinus congestion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	16 / 264 (6.06%)	12 / 267 (4.49%)
occurrences (all)	0	18	12
Insomnia			
subjects affected / exposed	1 / 9 (11.11%)	18 / 264 (6.82%)	22 / 267 (8.24%)
occurrences (all)	2	22	23
Disorientation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	1
Bradyphrenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 9 (33.33%)	41 / 264 (15.53%)	67 / 267 (25.09%)
occurrences (all)	7	69	99
Blood testosterone decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Amylase increased			
subjects affected / exposed	4 / 9 (44.44%)	22 / 264 (8.33%)	46 / 267 (17.23%)
occurrences (all)	14	30	73
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 9 (22.22%)	53 / 264 (20.08%)	76 / 267 (28.46%)
occurrences (all)	7	77	114
Blood albumin decreased			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	4 / 267 (1.50%)
occurrences (all)	1	1	4
Blood alkaline phosphatase increased			

subjects affected / exposed	2 / 9 (22.22%)	28 / 264 (10.61%)	33 / 267 (12.36%)
occurrences (all)	6	38	63
Blood cholesterol increased			
subjects affected / exposed	1 / 9 (11.11%)	11 / 264 (4.17%)	12 / 267 (4.49%)
occurrences (all)	2	23	29
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 9 (33.33%)	72 / 264 (27.27%)	75 / 267 (28.09%)
occurrences (all)	3	160	172
Blood creatinine increased			
subjects affected / exposed	2 / 9 (22.22%)	9 / 264 (3.41%)	24 / 267 (8.99%)
occurrences (all)	3	12	45
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 9 (11.11%)	21 / 264 (7.95%)	27 / 267 (10.11%)
occurrences (all)	4	41	44
Blood sodium decreased			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	1 / 267 (0.37%)
occurrences (all)	1	3	1
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	5 / 267 (1.87%)
occurrences (all)	1	2	5
Blood triglycerides increased			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	3 / 267 (1.12%)
occurrences (all)	1	4	6
C-reactive protein increased			
subjects affected / exposed	2 / 9 (22.22%)	11 / 264 (4.17%)	12 / 267 (4.49%)
occurrences (all)	3	13	12
Ejection fraction decreased			
subjects affected / exposed	1 / 9 (11.11%)	21 / 264 (7.95%)	18 / 267 (6.74%)
occurrences (all)	1	26	22
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 9 (22.22%)	20 / 264 (7.58%)	17 / 267 (6.37%)
occurrences (all)	5	25	22
Globulins increased			

subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 9 (0.00%)	5 / 264 (1.89%)	5 / 267 (1.87%)
occurrences (all)	0	5	6
Lipase increased			
subjects affected / exposed	5 / 9 (55.56%)	38 / 264 (14.39%)	66 / 267 (24.72%)
occurrences (all)	11	65	131
Lymphocyte count decreased			
subjects affected / exposed	0 / 9 (0.00%)	5 / 264 (1.89%)	5 / 267 (1.87%)
occurrences (all)	0	6	7
Myoglobin blood increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences (all)	1	0	3
Neutrophil count decreased			
subjects affected / exposed	2 / 9 (22.22%)	11 / 264 (4.17%)	8 / 267 (3.00%)
occurrences (all)	3	12	16
Transaminases increased			
subjects affected / exposed	0 / 9 (0.00%)	6 / 264 (2.27%)	9 / 267 (3.37%)
occurrences (all)	0	6	13
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)	11 / 264 (4.17%)	17 / 267 (6.37%)
occurrences (all)	0	12	25
White blood cell count decreased			
subjects affected / exposed	1 / 9 (11.11%)	6 / 264 (2.27%)	9 / 267 (3.37%)
occurrences (all)	1	6	12
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences (all)	1	2	2
Procedural pain			

subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences (all)	1	0	3
Radiation skin injury			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Anosmia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	2	1	0
Aphasia			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	4 / 267 (1.50%)
occurrences (all)	1	2	4
Dizziness			
subjects affected / exposed	2 / 9 (22.22%)	23 / 264 (8.71%)	21 / 267 (7.87%)
occurrences (all)	2	30	25
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	2 / 267 (0.75%)
occurrences (all)	0	4	2
Peroneal nerve palsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 9 (0.00%)	14 / 264 (5.30%)	14 / 267 (5.24%)
occurrences (all)	0	18	17
Migraine			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences (all)	1	2	6
Memory impairment			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	1 / 267 (0.37%)
occurrences (all)	1	2	1
Headache			
subjects affected / exposed	5 / 9 (55.56%)	74 / 264 (28.03%)	80 / 267 (29.96%)
occurrences (all)	31	188	208
Dysgeusia			
subjects affected / exposed	0 / 9 (0.00%)	6 / 264 (2.27%)	13 / 267 (4.87%)
occurrences (all)	0	6	14

Dysaesthesia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences (all)	0	2	2
Dizziness postural			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	2 / 9 (22.22%)	14 / 264 (5.30%)	23 / 267 (8.61%)
occurrences (all)	3	21	50
Anaemia			
subjects affected / exposed	4 / 9 (44.44%)	31 / 264 (11.74%)	49 / 267 (18.35%)
occurrences (all)	6	70	92
Lymphopenia			
subjects affected / exposed	1 / 9 (11.11%)	11 / 264 (4.17%)	20 / 267 (7.49%)
occurrences (all)	3	12	30
Thrombocytosis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	3 / 267 (1.12%)
occurrences (all)	1	2	3
Thrombocytopenia			
subjects affected / exposed	2 / 9 (22.22%)	10 / 264 (3.79%)	24 / 267 (8.99%)
occurrences (all)	2	23	43
Neutropenia			
subjects affected / exposed	4 / 9 (44.44%)	37 / 264 (14.02%)	44 / 267 (16.48%)
occurrences (all)	8	75	111
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	1
Ear pain			
subjects affected / exposed	3 / 9 (33.33%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences (all)	5	1	1
Motion sickness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Dry eye			
subjects affected / exposed	0 / 9 (0.00%)	9 / 264 (3.41%)	5 / 267 (1.87%)
occurrences (all)	0	13	6
Myopia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Iridocyclitis			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	3 / 267 (1.12%)
occurrences (all)	1	4	3
Ocular discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	0	0	1
Papilloedema			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences (all)	1	1	2
Vitreal cells			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 9 (0.00%)	6 / 264 (2.27%)	10 / 267 (3.75%)
occurrences (all)	0	7	10
Vision blurred			
subjects affected / exposed	0 / 9 (0.00%)	13 / 264 (4.92%)	9 / 267 (3.37%)
occurrences (all)	0	16	10
Uveitis			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	7 / 267 (2.62%)
occurrences (all)	3	5	8
Retinopathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Retinal haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	1
Photophobia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	6 / 267 (2.25%)
occurrences (all)	1	3	6

Periorbital oedema			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	4 / 267 (1.50%)
occurrences (all)	1	1	4
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 9 (11.11%)	5 / 264 (1.89%)	2 / 267 (0.75%)
occurrences (all)	1	6	2
Glossitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 9 (11.11%)	6 / 264 (2.27%)	9 / 267 (3.37%)
occurrences (all)	1	25	10
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	13 / 264 (4.92%)	18 / 267 (6.74%)
occurrences (all)	0	17	21
Dry mouth			
subjects affected / exposed	1 / 9 (11.11%)	13 / 264 (4.92%)	22 / 267 (8.24%)
occurrences (all)	1	14	26
Nausea			
subjects affected / exposed	1 / 9 (11.11%)	78 / 264 (29.55%)	90 / 267 (33.71%)
occurrences (all)	4	136	162
Constipation			
subjects affected / exposed	1 / 9 (11.11%)	40 / 264 (15.15%)	40 / 267 (14.98%)
occurrences (all)	2	49	55
Cheilitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 9 (11.11%)	17 / 264 (6.44%)	26 / 267 (9.74%)
occurrences (all)	2	29	39
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)	26 / 264 (9.85%)	29 / 267 (10.86%)
occurrences (all)	1	40	42
Diarrhoea			

subjects affected / exposed	4 / 9 (44.44%)	70 / 264 (26.52%)	98 / 267 (36.70%)
occurrences (all)	7	173	182
Vomiting			
subjects affected / exposed	4 / 9 (44.44%)	50 / 264 (18.94%)	69 / 267 (25.84%)
occurrences (all)	11	116	128
Odynophagia			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	4 / 267 (1.50%)
occurrences (all)	1	10	4
Trichoglossia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 9 (0.00%)	7 / 264 (2.65%)	5 / 267 (1.87%)
occurrences (all)	0	10	5
Hepatic function abnormal			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Hepatic steatosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	1
Hypertransaminasaemia			
subjects affected / exposed	2 / 9 (22.22%)	4 / 264 (1.52%)	6 / 267 (2.25%)
occurrences (all)	3	6	7
Immune-mediated hepatitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	1
Hepatitis			
subjects affected / exposed	2 / 9 (22.22%)	3 / 264 (1.14%)	5 / 267 (1.87%)
occurrences (all)	2	5	6
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	3 / 9 (33.33%)	14 / 264 (5.30%)	13 / 267 (4.87%)
occurrences (all)	5	16	14
Dry skin			

subjects affected / exposed	0 / 9 (0.00%)	15 / 264 (5.68%)	14 / 267 (5.24%)
occurrences (all)	0	15	17
Alopecia			
subjects affected / exposed	0 / 9 (0.00%)	9 / 264 (3.41%)	17 / 267 (6.37%)
occurrences (all)	0	9	17
Eczema			
subjects affected / exposed	1 / 9 (11.11%)	16 / 264 (6.06%)	9 / 267 (3.37%)
occurrences (all)	1	19	10
Erythema			
subjects affected / exposed	0 / 9 (0.00%)	11 / 264 (4.17%)	27 / 267 (10.11%)
occurrences (all)	0	12	37
Photosensitivity reaction			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	9 / 267 (3.37%)
occurrences (all)	1	3	12
Panniculitis			
subjects affected / exposed	1 / 9 (11.11%)	8 / 264 (3.03%)	9 / 267 (3.37%)
occurrences (all)	3	12	15
Palmoplantar keratoderma			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences (all)	1	4	0
Night sweats			
subjects affected / exposed	3 / 9 (33.33%)	11 / 264 (4.17%)	10 / 267 (3.75%)
occurrences (all)	4	18	26
Ingrowing nail			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	3 / 267 (1.12%)
occurrences (all)	1	1	3
Hyperkeratosis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	5 / 267 (1.87%)
occurrences (all)	1	1	7
Hyperhidrosis			
subjects affected / exposed	2 / 9 (22.22%)	14 / 264 (5.30%)	7 / 267 (2.62%)
occurrences (all)	12	15	7
Granuloma annulare			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	1	1	0
Erythema nodosum			

subjects affected / exposed	1 / 9 (11.11%)	9 / 264 (3.41%)	14 / 267 (5.24%)
occurrences (all)	6	12	14
Pruritus			
subjects affected / exposed	1 / 9 (11.11%)	22 / 264 (8.33%)	51 / 267 (19.10%)
occurrences (all)	3	26	89
Skin disorder			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	2	1	0
Sensitive skin			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	1 / 267 (0.37%)
occurrences (all)	1	4	2
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	7 / 267 (2.62%)
occurrences (all)	0	1	8
Stasis dermatitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences (all)	1	1	3
Rash macular			
subjects affected / exposed	2 / 9 (22.22%)	3 / 264 (1.14%)	2 / 267 (0.75%)
occurrences (all)	2	4	2
Rash erythematous			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	5 / 267 (1.87%)
occurrences (all)	1	1	5
Rash			
subjects affected / exposed	4 / 9 (44.44%)	68 / 264 (25.76%)	76 / 267 (28.46%)
occurrences (all)	11	97	115
Psoriasis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences (all)	0	1	1
Rash maculo-papular			
subjects affected / exposed	2 / 9 (22.22%)	6 / 264 (2.27%)	16 / 267 (5.99%)
occurrences (all)	2	39	21
Urticaria			

subjects affected / exposed	1 / 9 (11.11%)	7 / 264 (2.65%)	6 / 267 (2.25%)
occurrences (all)	3	7	6
Vitiligo			
subjects affected / exposed	0 / 9 (0.00%)	3 / 264 (1.14%)	21 / 267 (7.87%)
occurrences (all)	0	3	21
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 9 (0.00%)	8 / 264 (3.03%)	14 / 267 (5.24%)
occurrences (all)	0	11	19
Haematuria			
subjects affected / exposed	1 / 9 (11.11%)	9 / 264 (3.41%)	8 / 267 (3.00%)
occurrences (all)	1	9	8
Nocturia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	0	1	0
Acute kidney injury			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	6 / 267 (2.25%)
occurrences (all)	1	1	8
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	1 / 267 (0.37%)
occurrences (all)	1	0	1
Hyperthyroidism			
subjects affected / exposed	2 / 9 (22.22%)	5 / 264 (1.89%)	18 / 267 (6.74%)
occurrences (all)	2	5	22
Hypothyroidism			
subjects affected / exposed	4 / 9 (44.44%)	17 / 264 (6.44%)	20 / 267 (7.49%)
occurrences (all)	4	19	24
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Thyroiditis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	3 / 267 (1.12%)
occurrences (all)	1	0	3
Musculoskeletal and connective tissue disorders			

Groin pain			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	7 / 267 (2.62%)
occurrences (all)	1	1	7
Flank pain			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	1 / 267 (0.37%)
occurrences (all)	1	2	1
Back pain			
subjects affected / exposed	2 / 9 (22.22%)	37 / 264 (14.02%)	33 / 267 (12.36%)
occurrences (all)	2	49	40
Arthritis			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	6 / 267 (2.25%)
occurrences (all)	1	4	6
Arthralgia			
subjects affected / exposed	6 / 9 (66.67%)	80 / 264 (30.30%)	87 / 267 (32.58%)
occurrences (all)	35	155	165
Joint swelling			
subjects affected / exposed	1 / 9 (11.11%)	5 / 264 (1.89%)	6 / 267 (2.25%)
occurrences (all)	3	5	6
Limb discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences (all)	1	0	3
Musculoskeletal stiffness			
subjects affected / exposed	1 / 9 (11.11%)	5 / 264 (1.89%)	1 / 267 (0.37%)
occurrences (all)	2	5	1
Musculoskeletal pain			
subjects affected / exposed	0 / 9 (0.00%)	8 / 264 (3.03%)	3 / 267 (1.12%)
occurrences (all)	0	11	3
Musculoskeletal chest pain			
subjects affected / exposed	2 / 9 (22.22%)	3 / 264 (1.14%)	5 / 267 (1.87%)
occurrences (all)	2	5	6
Muscular weakness			
subjects affected / exposed	0 / 9 (0.00%)	4 / 264 (1.52%)	8 / 267 (3.00%)
occurrences (all)	0	4	9
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)	28 / 264 (10.61%)	32 / 267 (11.99%)
occurrences (all)	0	36	68

Myalgia			
subjects affected / exposed	4 / 9 (44.44%)	37 / 264 (14.02%)	43 / 267 (16.10%)
occurrences (all)	6	83	71
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	9 / 264 (3.41%)	7 / 267 (2.62%)
occurrences (all)	0	9	7
Osteopenia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	1	1	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	23 / 264 (8.71%)	31 / 267 (11.61%)
occurrences (all)	1	30	48
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	5 / 264 (1.89%)	20 / 267 (7.49%)
occurrences (all)	0	5	22
Candida infection			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	0 / 267 (0.00%)
occurrences (all)	2	2	0
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)	13 / 264 (4.92%)	18 / 267 (6.74%)
occurrences (all)	0	13	20
Cellulitis			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	6 / 267 (2.25%)
occurrences (all)	1	3	8
Gastrointestinal viral infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	1	1	0
Furuncle			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	0 / 267 (0.00%)
occurrences (all)	1	3	0
Fungal skin infection			

subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	2 / 267 (0.75%)
occurrences (all)	1	1	2
Folliculitis			
subjects affected / exposed	3 / 9 (33.33%)	8 / 264 (3.03%)	14 / 267 (5.24%)
occurrences (all)	5	10	19
Conjunctivitis			
subjects affected / exposed	2 / 9 (22.22%)	9 / 264 (3.41%)	14 / 267 (5.24%)
occurrences (all)	2	9	15
Nasopharyngitis			
subjects affected / exposed	2 / 9 (22.22%)	32 / 264 (12.12%)	28 / 267 (10.49%)
occurrences (all)	2	39	44
Oral candidiasis			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences (all)	1	2	3
Tonsillitis			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	3 / 267 (1.12%)
occurrences (all)	1	2	3
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	12 / 267 (4.49%)
occurrences (all)	1	3	15
Rhinitis			
subjects affected / exposed	1 / 9 (11.11%)	10 / 264 (3.79%)	18 / 267 (6.74%)
occurrences (all)	1	11	20
Postoperative wound infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	0 / 267 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	9 / 264 (3.41%)	9 / 267 (3.37%)
occurrences (all)	1	10	10
Paronychia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	4 / 267 (1.50%)
occurrences (all)	1	4	5
Otitis media chronic			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Otitis media			

subjects affected / exposed	1 / 9 (11.11%)	1 / 264 (0.38%)	1 / 267 (0.37%)
occurrences (all)	1	1	1
Oral herpes			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	8 / 267 (3.00%)
occurrences (all)	1	4	10
Upper respiratory tract infection			
subjects affected / exposed	3 / 9 (33.33%)	9 / 264 (3.41%)	17 / 267 (6.37%)
occurrences (all)	4	10	30
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	2 / 264 (0.76%)	2 / 267 (0.75%)
occurrences (all)	1	3	2
Viral rhinitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	1	0	0
Viral pharyngitis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 264 (0.00%)	0 / 267 (0.00%)
occurrences (all)	3	0	0
Viral infection			
subjects affected / exposed	1 / 9 (11.11%)	5 / 264 (1.89%)	4 / 267 (1.50%)
occurrences (all)	1	5	5
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	25 / 264 (9.47%)	26 / 267 (9.74%)
occurrences (all)	0	39	55
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 9 (22.22%)	27 / 264 (10.23%)	33 / 267 (12.36%)
occurrences (all)	2	30	38
Dehydration			
subjects affected / exposed	1 / 9 (11.11%)	3 / 264 (1.14%)	3 / 267 (1.12%)
occurrences (all)	1	4	3
Hypophosphataemia			
subjects affected / exposed	0 / 9 (0.00%)	16 / 264 (6.06%)	14 / 267 (5.24%)
occurrences (all)	0	25	21
Hyperglycaemia			
subjects affected / exposed	1 / 9 (11.11%)	24 / 264 (9.09%)	37 / 267 (13.86%)
occurrences (all)	1	35	92

Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	4 / 264 (1.52%)	3 / 267 (1.12%)
occurrences (all)	0	4	3
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)	6 / 264 (2.27%)	15 / 267 (5.62%)
occurrences (all)	2	7	27
Hyponatraemia			
subjects affected / exposed	2 / 9 (22.22%)	4 / 264 (1.52%)	17 / 267 (6.37%)
occurrences (all)	3	5	30
Hypercholesterolaemia			
subjects affected / exposed	1 / 9 (11.11%)	4 / 264 (1.52%)	8 / 267 (3.00%)
occurrences (all)	1	10	14
Iron deficiency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 264 (0.00%)	2 / 267 (0.75%)
occurrences (all)	1	0	2
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 9 (11.11%)	5 / 264 (1.89%)	1 / 267 (0.37%)
occurrences (all)	1	5	1

Non-serious adverse events	Part II PDR001 + D + T		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 27 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibrous histiocytoma			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Basal cell carcinoma			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	4		
Superficial vein thrombosis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		

Hypotension subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Lymphoedema subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3		
Orthostatic hypotension subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Hypertension subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
General disorders and administration site conditions Face oedema subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Fatigue subjects affected / exposed occurrences (all)	11 / 27 (40.74%) 15		
Influenza like illness subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 5		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Oedema subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 3		
Oedema due to cardiac disease subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	9 / 27 (33.33%) 44		
Axillary pain			

subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	11 / 27 (40.74%)		
occurrences (all)	17		
Oedema peripheral			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	6		
Pyrexia			
subjects affected / exposed	23 / 27 (85.19%)		
occurrences (all)	99		
Xerosis			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Sarcoidosis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Cough			
subjects affected / exposed	12 / 27 (44.44%)		
occurrences (all)	15		
Epistaxis			

subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Pleurisy			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Pneumonitis			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	5		
Pulmonary embolism			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Pulmonary haemorrhage			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Disorientation			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Bradyphrenia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences (all)	12		
Blood testosterone decreased			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Amylase increased			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	13		
Blood albumin decreased			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	8		
Blood cholesterol increased			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	5		
Blood creatine phosphokinase increased			
subjects affected / exposed	9 / 27 (33.33%)		
occurrences (all)	13		
Blood creatinine increased			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	4		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Blood sodium decreased			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Blood thyroid stimulating hormone			

decreased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Blood triglycerides increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
C-reactive protein increased				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			
Ejection fraction decreased				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			
Gamma-glutamyltransferase increased				
subjects affected / exposed	3 / 27 (11.11%)			
occurrences (all)	3			
Globulins increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Hepatic enzyme increased				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			
Lipase increased				
subjects affected / exposed	5 / 27 (18.52%)			
occurrences (all)	8			
Lymphocyte count decreased				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			
Myoglobin blood increased				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	3 / 27 (11.11%)			
occurrences (all)	4			
Transaminases increased				

subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
White blood cell count decreased			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Radiation skin injury			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Anosmia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Aphasia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
Peroneal nerve palsy			

subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	8		
Migraine			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	8 / 27 (29.63%)		
occurrences (all)	18		
Dysgeusia			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Dysaesthesia			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Dizziness postural			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	3		
Anaemia			
subjects affected / exposed	10 / 27 (37.04%)		
occurrences (all)	13		
Lymphopenia			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	11		
Thrombocytosis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		

Thrombocytopenia			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	7		
Neutropenia			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	11		
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Motion sickness			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	9 / 27 (33.33%)		
occurrences (all)	9		
Myopia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Iridocyclitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Ocular discomfort			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Papilloedema			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Vitreal cells			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Visual impairment			

subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Vision blurred			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Uveitis			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Retinopathy			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Retinal haemorrhage			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Photophobia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Periorbital oedema			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Glossitis			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	6 / 27 (22.22%)		
occurrences (all)	8		

Nausea			
subjects affected / exposed	8 / 27 (29.63%)		
occurrences (all)	19		
Constipation			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences (all)	10		
Cheilitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	10		
Diarrhoea			
subjects affected / exposed	9 / 27 (33.33%)		
occurrences (all)	14		
Vomiting			
subjects affected / exposed	10 / 27 (37.04%)		
occurrences (all)	14		
Odynophagia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Trichoglossia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Hepatic function abnormal			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Hepatic steatosis			

subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Hypertransaminasaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Immune-mediated hepatitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Hepatitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	7		
Alopecia			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	3		
Erythema			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Photosensitivity reaction			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Panniculitis			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Palmoplantar keratoderma			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		

Night sweats				
subjects affected / exposed	4 / 27 (14.81%)			
occurrences (all)	5			
Ingrowing nail				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Hyperkeratosis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Hyperhidrosis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	1			
Granuloma annulare				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Erythema nodosum				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	2			
Pruritus				
subjects affected / exposed	8 / 27 (29.63%)			
occurrences (all)	12			
Skin disorder				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Sensitive skin				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Seborrhoeic dermatitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Rash pruritic				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			
Stasis dermatitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			

Rash macular subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 3		
Rash erythematous subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Rash subjects affected / exposed occurrences (all)	13 / 27 (48.15%) 20		
Psoriasis subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 4		
Rash maculo-papular subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3		
Urticaria subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Vitiligo subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Haematuria subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Nocturia subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Acute kidney injury subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Endocrine disorders			

Hypophysitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Hyperthyroidism			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Thyroiditis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	8		
Arthritis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	15 / 27 (55.56%)		
occurrences (all)	26		
Joint swelling			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	4		
Limb discomfort			

subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	8 / 27 (29.63%)		
occurrences (all)	11		
Neck pain			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	4		
Osteopenia			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Rotator cuff syndrome			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	6 / 27 (22.22%)		
occurrences (all)	11		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		

Candida infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
COVID-19				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Cellulitis				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	3			
Gastrointestinal viral infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	1			
Fungal skin infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Folliculitis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	2			
Conjunctivitis				
subjects affected / exposed	3 / 27 (11.11%)			
occurrences (all)	4			
Nasopharyngitis				
subjects affected / exposed	3 / 27 (11.11%)			
occurrences (all)	3			
Oral candidiasis				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			
Tonsillitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	2			

Rhinitis				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	1			
Postoperative wound infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	2 / 27 (7.41%)			
occurrences (all)	4			
Paronychia				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Otitis media chronic				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Otitis media				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	1			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Viral rhinitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Viral pharyngitis				
subjects affected / exposed	0 / 27 (0.00%)			
occurrences (all)	0			
Viral infection				
subjects affected / exposed	1 / 27 (3.70%)			
occurrences (all)	1			

Urinary tract infection subjects affected / exposed occurrences (all)	5 / 27 (18.52%) 5		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	7 / 27 (25.93%) 9		
Dehydration subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 9		
Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 3		
Hypocalcaemia subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 3		
Hyponatraemia subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Iron deficiency subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2017	• Removed double barrier contraception from the list of highly effective methods of contraception and clarified this removal from the exclusion criterion.
07 March 2017	• Updated criteria for DLT for Part 1. • Added '≥ grade 3 AEs that were known to occur with dabrafenib, trametinib and/or spartalizumab, but cannot be controlled using the recommended product-specific management guidelines or lead to 50% of planned exposure to study medications'. • Changed threshold for subjects with normal baseline AST and ALT values: 'AST or ALT > 8.0 × ULN' (grade 4 AST or ALT elevation' was subsequently removed) • 'Active infection requiring systemic antibiotic therapy within 2 weeks prior to start of study treatment' • Added requirement for a local HIV testing at screening for subjects in Germany to exclusion criterion • Updated primary objective and endpoint for Part 2 to specifically mention the main two biomarkers of interest (PD-L1 levels and CD+8 cells).
14 July 2017	• Changes were made to pyrexia management guidelines based on the safety profile observed in the safety run-in (part 1) and feedback received from investigators upon review of safety data. • Changes to improve data collection for radiotherapy events, central review using tumor response criteria based on guidelines for immunotherapy, ophthalmologic examination assessment frequency, and patient reported outcomes were implemented • The BRAF V600 testing method was clarified and language was added to reflect the AJCC edition 8 melanoma staging system • The frequency of the data monitoring committee review of safety data was revised from 6 to 3-6 months to ensure appropriate safety monitoring
14 August 2018	• Aligned the contraception requirements during and after study treatment based on the dabrafenib Investigator's Brochure (IB) Edition 10 and trametinib IB Edition 9. • The safety follow-up periods were aligned with the contraception requirements after study treatment had been discontinued. • Revised individual subject unblinding requirements to limit the impact of unblinding on the scientific validity of the study results • Added a new exploratory objective and a corresponding endpoint to characterize the potential for TMB alone and in combination with PD-L1, or additional markers to identify subjects with an enhanced response to spartalizumab in combination with dabrafenib and trametinib versus placebo plus dabrafenib and trametinib. • Updated withdrawal of consent to reflect European Economic Area General Data Protection Regulation requirements. Except for US and Japan, all biological samples not yet analyzed at the time of withdrawal were no longer to be used for analysis.
08 March 2019	• Adjusted the timing of the final PFS analysis and included an interim analysis for PFS based on revised assumptions on the delayed treatment effect. • In order to achieve a statistical power of 80% based on a conservative assumption of a 5 months delayed treatment effect and followed by an effect of the same magnitude as assumed in the original protocol (i.e. HR=0.60), the number of PFS events for the final PFS analysis was increased from 246 to approximately 352 PFS events. Furthermore, an interim PFS analysis was introduced at approximately 260 PFS events. • In addition, OS analysis was also revised based on the assumed 5 months delayed treatment effect.

13 October 2020	• The primary objective of this amendment was to enable continuation of the study following the final PFS analysis, in order to characterize the overall survival benefit observed at the final PFS analysis. • Removal of the crossover schedule as it was no longer applicable as protocol defined criteria for crossover was not met. • Inclusion of all general recommendations already provided to the investigators in a letter dated 7-Apr-2020 to provide guidance on coronavirus disease-19 (COVID-19) related challenges that may affected the study protocol execution. • The contraception information was updated.
18 January 2023	• Revised the definition of end of study in section 4.3 of the protocol to include Post-Trial Access (PTA) program i.e., rollover protocol or a post study drug supply (PSDS) option for subjects still on study treatment and in the opinion of the investigator still deriving clinical benefit at the time of end of the study. • Updated safety information on hemophagocytic lymphohistiocytosis (HLH) and updated "dose modification and recommended clinical management guidelines" in the safety section including treatment resumption for recurrent grade 4 asymptomatic amylase or lipase elevation per UK Health Authority (MHRA) request. • A sub-section 2.7 related to public health emergency mitigation procedures was added. • Section 8.3 related to "Emergency unblinding of treatment assignment" was updated for clarification per Swissmedic feedback. • Language was updated to align with the latest Novartis protocol template (OneCTP version 5.0).

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 go to https://www.novctrd.com/#/ for complete trial results

Notes: