Clinical trial results:
A Randomized Phase 3 Open Label Study of Nivolumab versus Bevacizumab and a Safety Study of Nivolumab or Nivolumab in Combination with Ipilimumab in Adult Subjects with Recurrent Glioblastoma (GBM) (CheckMate 143: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 143).

Summary

EudraCT number	2013-003738-34
Trial protocol	DE IT ES BE DK PL FR NL
Global end of trial date	21 June 2024

Results information

Result version number	v1 (current)
This version publication date	02 April 2025
First version publication date	02 April 2025

Trial information

Trial identification

Sponsor protocol code	CA209-143

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management, Clinical Trials, Bristol-Myers Squibb, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@bms.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	18 July 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Cohort 1 and 1b (Safety Lead-in):
To evaluate the safety and tolerability of nivolumab and nivolumab in combination with ipilimumab
Cohort 2:
To compare the overall survival (OS) of nivolumab versus bevacizumab.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 2014
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	Australia: 24
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 44
Country: Number of subjects enrolled	Italy: 75
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Switzerland: 13
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	United States: 301
Worldwide total number of subjects	529
EEA total number of subjects	179

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)	414
From 65 to 84 years	115
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

529 participants participated in the study. 4 (81 directly treated, 423 randomized and treated).

GBM = Glioblastoma
MGMT = O6-methylguanin-DNA-methyltransferase

Period 1

Period 1 title	Before treatment period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Arm N1+I3

Arm description:

Nivolumab 1 mg/kg administered as a 60-minute intravenous (IV) infusion followed by ipilimumab 3 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

1 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Cohort 1: Arm N3

Arm description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks

Arm type	Experimental

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Cohort 1b: Arm N3+I1

Arm description:

Nivolumab 3 mg/kg administered as a 60-minute IV infusion followed by ipilimumab 1 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

1 mg/kg

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Part A Cohort 1c: Arm N3+RT+TMZ

Arm description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Part A Cohort 1d: Arm N3+RT

Arm description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Part B Cohort 1c: Arm N3+RT+TMZ

Arm description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Part B Cohort 1d: Arm N3+RT

Arm description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Cohort 2: Arm N3

Arm description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Cohort 2: Arm B

Arm description:

Bevacizumab 10 mg/kg dosed every 2 weeks as 90-minute IV infusion for the first dose and 60-minute IV infusions for subsequent doses if the first infusion is tolerated

Arm type	Active comparator
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg

Number of subjects in period 1	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1
Started	10	10	20
Randomized	10	10	0 [1]
Completed	10	10	20
Not completed	0	0	0
Participant no longer met criteria	-	-	-
Adverse Event unrelated to study drug	-	-	-
Participant withdrew consent	-	-	-
Participant request to stop therapy	-	-	-
Lost to follow-up	-	-	-
other reason	-	-	-

Number of subjects in period 1	Part A Cohort 1c: Arm N3+RT+TMZ	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ
Started	31	30	29
Randomized	0 [2]	0 [3]	29
Completed	31	30	28
Not completed	0	0	1
Participant no longer met criteria	-	-	1
Adverse Event unrelated to study drug	-	-	-
Participant withdrew consent	-	-	-
Participant request to stop therapy	-	-	-
Lost to follow-up	-	-	-
other reason	-	-	-

Number of subjects in period 1	Part B Cohort 1d: Arm N3+RT	Cohort 2: Arm N3	Cohort 2: Arm B
Started	30	184	185
Randomized	30	184	185
Completed	28	182	165
Not completed	2	2	20
Participant no longer met criteria	-	1	2
Adverse Event unrelated to study drug	-	1	-
Participant withdrew consent	2	-	11
Participant request to stop therapy	-	-	5
Lost to follow-up	-	-	1
other reason	-	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 81 participants were not randomized but directly treated.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 81 participants were not randomized but directly treated.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 81 participants were not randomized but directly treated.

Period 2

Period 2 title	Treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Arm N1+I3

Arm description:

Nivolumab 1 mg/kg administered as a 60-minute intravenous (IV) infusion followed by ipilimumab 3 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

1 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

1 mg/kg

Arm title	Cohort 1: Arm N3

Arm description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details: 3 mg/kg	

Arm title	Cohort 1b: Arm N3+I1
Arm description: Nivolumab 3 mg/kg administered as a 60-minute IV infusion followed by ipilimumab 1 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use
Dosage and administration details: 1 mg/kg	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use
Dosage and administration details: 3 mg/kg	
Arm title	Part A Cohort 1c: Arm N3+RT+TMZ
Arm description: Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide	
Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use
Dosage and administration details: 3 mg/kg	
Arm title	Part A Cohort 1d: Arm N3+RT
Arm description: Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy	
Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use
Dosage and administration details: 3 mg/kg	
Arm title	Part B Cohort 1c: Arm N3+RT+TMZ

Arm description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Part B Cohort 1d: Arm N3+RT

Arm description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Cohort 2: Arm N3

Arm description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

3 mg/kg

Arm title	Cohort 2: Arm B

Arm description:

Bevacizumab 10 mg/kg dosed every 2 weeks as 90-minute IV infusion for the first dose and 60-minute IV infusions for subsequent doses if the first infusion is tolerated

Arm type	Active comparator
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg

Number of subjects in period 2	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1
Started	10	10	20
Completed	0	0	0
Not completed	10	10	20
Adverse event, serious fatal	-	-	1
Participant no longer met criteria	-	-	-
Disease progression	7	9	12
Adverse Event unrelated to study drug	-	-	2
Participant withdrew consent	-	-	1
Study drug toxicity	3	-	1
Not reported	-	1	-
Maximum clinical benefit	-	-	-
Other reasons	-	-	-
Participant request to stop therapy	-	-	3

Number of subjects in period 2	Part A Cohort 1c: Arm N3+RT+TMZ	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ
Started	31	30	28
Completed	0	0	0
Not completed	31	30	28
Adverse event, serious fatal	-	-	2
Participant no longer met criteria	-	-	-
Disease progression	20	26	16
Adverse Event unrelated to study drug	-	-	-
Participant withdrew consent	-	-	2
Study drug toxicity	4	4	5
Not reported	-	-	-
Maximum clinical benefit	-	-	-
Other reasons	1	-	1
Participant request to stop therapy	6	-	2

Number of subjects in period 2	Part B Cohort 1d: Arm N3+RT	Cohort 2: Arm N3	Cohort 2: Arm B
Started	28	182	165
Completed	0	0	0
Not completed	28	182	165
Adverse event, serious fatal	-	-	-
Participant no longer met criteria	-	-	1
Disease progression	22	165	135
Adverse Event unrelated to study drug	1	4	5
Participant withdrew consent	-	1	4

Study drug toxicity	3	7	11
Not reported	-	-	-
Maximum clinical benefit	-	-	1
Other reasons	1	1	1
Participant request to stop therapy	1	4	7

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Arm N1+I3
Reporting group description:	
Nivolumab 1 mg/kg administered as a 60-minute intravenous (IV) infusion followed by ipilimumab 3 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Reporting group title	Cohort 1: Arm N3
Reporting group description:	
Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks	
Reporting group title	Cohort 1b: Arm N3+I1
Reporting group description:	
Nivolumab 3 mg/kg administered as a 60-minute IV infusion followed by ipilimumab 1 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Reporting group title	Part A Cohort 1c: Arm N3+RT+TMZ
Reporting group description:	
Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide	
Reporting group title	Part A Cohort 1d: Arm N3+RT
Reporting group description:	
Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy	
Reporting group title	Part B Cohort 1c: Arm N3+RT+TMZ
Reporting group description:	
Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide	
Reporting group title	Part B Cohort 1d: Arm N3+RT
Reporting group description:	
Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy	
Reporting group title	Cohort 2: Arm N3
Reporting group description:	
Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks	
Reporting group title	Cohort 2: Arm B
Reporting group description:	
Bevacizumab 10 mg/kg dosed every 2 weeks as 90-minute IV infusion for the first dose and 60-minute IV infusions for subsequent doses if the first infusion is tolerated	

Reporting group values	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1
Number of subjects	10	10	20
Age Categorical Units: Participants			
< 65	7	6	17
>= 65	3	4	3
Age Continuous Units: Years			
arithmetic mean	54.5	58.6	55.0

standard deviation	± 11.3	± 10.9	± 11.9

Sex: Female, Male Units: Participants			
Female	4	5	6
Male	6	5	14
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	10	10	20
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Black or African American	0	2	0
White	10	8	18
Other	0	0	1
Not Reported	0	0	0

Reporting group values	Part A Cohort 1c: Arm N3+RT+TMZ	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ
Number of subjects	31	30	29
Age Categorical Units: Participants			
< 65	23	22	22
>= 65	8	8	7
Age Continuous Units: Years			
arithmetic mean	56.5	58.2	57.3
standard deviation	± 11.3	± 10.2	± 12.7
Sex: Female, Male Units: Participants			
Female	11	8	10
Male	20	22	19
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	1
Not Hispanic or Latino	29	27	28
Unknown or Not Reported	0	1	0
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	0	1
Black or African American	2	0	0
White	26	28	27
Other	2	1	1
Not Reported	0	0	0

Reporting group values	Part B Cohort 1d: Arm N3+RT	Cohort 2: Arm N3	Cohort 2: Arm B
Number of subjects	30	184	185
Age Categorical Units: Participants			
< 65	19	142	156
>= 65	11	42	29
Age Continuous Units: Years			
arithmetic mean	58.8	55.0	54.2
standard deviation	± 10.5	± 11.3	± 10.7
Sex: Female, Male Units: Participants			
Female	9	68	66
Male	21	116	119
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	4	1
Not Hispanic or Latino	29	86	88
Unknown or Not Reported	1	94	96
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	1
Black or African American	0	2	2
White	28	176	181
Other	0	4	1
Not Reported	1	0	0

Reporting group values	Total		
Number of subjects	529		
Age Categorical Units: Participants			
< 65	414		
>= 65	115		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	187		
Male	342		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	10		
Not Hispanic or Latino	327		
Unknown or Not Reported	192		
Race/Ethnicity, Customized			
Race only			

Units: Subjects			
American Indian or Alaska Native	1		
Asian	7		
Black or African American	8		
White	502		
Other	10		
Not Reported	1		

End points

End points reporting groups

Reporting group title	Cohort 1: Arm N1+I3
Reporting group description:	
Nivolumab 1 mg/kg administered as a 60-minute intravenous (IV) infusion followed by ipilimumab 3 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Reporting group title	Cohort 1: Arm N3
Reporting group description:	
Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks	
Reporting group title	Cohort 1b: Arm N3+I1
Reporting group description:	
Nivolumab 3 mg/kg administered as a 60-minute IV infusion followed by ipilimumab 1 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Reporting group title	Part A Cohort 1c: Arm N3+RT+TMZ
Reporting group description:	
Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide	
Reporting group title	Part A Cohort 1d: Arm N3+RT
Reporting group description:	
Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy	
Reporting group title	Part B Cohort 1c: Arm N3+RT+TMZ
Reporting group description:	
Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide	
Reporting group title	Part B Cohort 1d: Arm N3+RT
Reporting group description:	
Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy	
Reporting group title	Cohort 2: Arm N3
Reporting group description:	
Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks	
Reporting group title	Cohort 2: Arm B
Reporting group description:	
Bevacizumab 10 mg/kg dosed every 2 weeks as 90-minute IV infusion for the first dose and 60-minute IV infusions for subsequent doses if the first infusion is tolerated	
Reporting group title	Cohort 1: Arm N1+I3
Reporting group description:	
Nivolumab 1 mg/kg administered as a 60-minute intravenous (IV) infusion followed by ipilimumab 3 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Reporting group title	Cohort 1: Arm N3
Reporting group description:	
Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks	
Reporting group title	Cohort 1b: Arm N3+I1
Reporting group description:	
Nivolumab 3 mg/kg administered as a 60-minute IV infusion followed by ipilimumab 1 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter	
Reporting group title	Part A Cohort 1c: Arm N3+RT+TMZ

Reporting group description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide

Reporting group title	Part A Cohort 1d: Arm N3+RT

Reporting group description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy

Reporting group title	Part B Cohort 1c: Arm N3+RT+TMZ

Reporting group description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide

Reporting group title	Part B Cohort 1d: Arm N3+RT

Reporting group description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy

Reporting group title	Cohort 2: Arm N3

Reporting group description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks

Reporting group title	Cohort 2: Arm B

Reporting group description:

Bevacizumab 10 mg/kg dosed every 2 weeks as 90-minute IV infusion for the first dose and 60-minute IV infusions for subsequent doses if the first infusion is tolerated

Primary: Percentage of Participants with Drug-Related Adverse Events Leading to Discontinuation by Worst CTC Grade for All Treated Participants in Cohorts 1, 1b, 1c and 1d Who Permanently Discontinued Study Medication Prior to Completing Four Doses

End point title	Percentage of Participants with Drug-Related Adverse Events Leading to Discontinuation by Worst CTC Grade for All Treated Participants in Cohorts 1, 1b, 1c and 1d Who Permanently Discontinued Study Medication Prior to Completing Four Doses[1][2]

End point description:

The percentage of participants who experienced a drug-related adverse event leading to drug discontinuation by worst grade (grade 5 being the worst) prior to complete four-dose treatment. Toxicities were graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. MedDRA Version: 24.1

End point type	Primary

End point timeframe:

Includes events reported between first dose and 30 days after last dose of study therapy (up to 3 doses, up to approximately 2 months)

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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

[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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

End point values	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1	Part A Cohort 1c: Arm N3+RT+TMZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	7	3
Units: Percentage of participants				
number (not applicable)				
Grade 1	0	0	0	0
Grade 2	0	0	0	0
Grade 3	16.7	0	0	66.7
Grade 4	33.3	0	0	0
Grade 5	0	0	0	0

End point values	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ	Part B Cohort 1d: Arm N3+RT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	4	4	
Units: Percentage of participants				
number (not applicable)				
Grade 1	0	0	0	
Grade 2	0	0	0	
Grade 3	0	0	50.0	
Grade 4	0	0	0	
Grade 5	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Adverse Events (Worst Grade) in Cohorts 1, 1b, 1c and 1d

End point title	Percentage of Participants with Adverse Events (Worst Grade) in Cohorts 1, 1b, 1c and 1d[3][4]

End point description:

The percentage of participants who experienced an adverse event by worst grade in each treatment arm. Toxicities were graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. MedDRA Version: 24.1

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to approximately 34 months).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

[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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

End point values	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1	Part A Cohort 1c: Arm N3+RT+TMZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	20	31
Units: Percentage of participants				
number (not applicable)				
Grade 1	0	20.0	5.0	6.5
Grade 2	10.0	30.0	25.0	12.9
Grade 3	70.0	40.0	50.0	58.1
Grade 4	20.0	10.0	20.0	22.6
Grade 5	0	0	0	0

End point values	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ	Part B Cohort 1d: Arm N3+RT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	28	28	
Units: Percentage of participants				
number (not applicable)				
Grade 1	13.3	3.6	17.9	
Grade 2	26.7	28.6	25.0	
Grade 3	33.3	50.0	35.7	
Grade 4	20.0	10.7	21.4	
Grade 5	3.3	3.6	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Serious Adverse Events (Worst Grade) in Cohorts 1, 1b, 1c and 1d

End point title	Percentage of Participants with Serious Adverse Events (Worst Grade) in Cohorts 1, 1b, 1c and 1d[5][6]

End point description:

The percentage of participants who experienced a serious adverse event by worst grade in each treatment arm. Toxicities were graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. MedDRA Version: 24.1

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to approximately 34 months).

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

[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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

End point values	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1	Part A Cohort 1c: Arm N3+RT+TMZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	20	31
Units: Percentage of participants				
number (not applicable)				
Grade 1	0	0	0	3.2
Grade 2	0	10.0	5.0	0
Grade 3	60.0	40.0	35.0	45.2
Grade 4	20.0	0	15.0	16.1
Grade 5	0	0	0	0

End point values	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ	Part B Cohort 1d: Arm N3+RT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	28	28	
Units: Percentage of participants				
number (not applicable)				
Grade 1	0	0	0	
Grade 2	16.7	3.6	10.7	
Grade 3	16.7	35.7	32.1	
Grade 4	16.7	3.6	14.3	
Grade 5	3.3	3.6	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Specific Laboratory Abnormalities in Liver Tests in Cohorts 1, 1b, 1c and 1d

End point title	Percentage of Participants with Specific Laboratory Abnormalities in Liver Tests in Cohorts 1, 1b, 1c and 1d[7][8]

End point description:

The percentage of participants who experienced a laboratory abnormality of the liver in each treatment arm.

MedDRA Version: 24.1

Aspartate aminotransferase (AST) Alanine aminotransferase (ALT) Upper Limit of Normal (ULN) Denominator corresponds to participants with at least on one treatment measurement of the corresponding laboratory parameter. Includes laboratory results reported after the first dose and within 30 days of last dose of study therapy.

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to approximately 34 months).

Notes:

[7] - 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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

[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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

End point values	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1	Part A Cohort 1c: Arm N3+RT+TMZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	19	31
Units: Percentage of participants				
number (not applicable)				
ALT OR AST > 3*ULN	30.0	0.0	15.8	22.6
ALT OR AST > 5*ULN	20.0	0.0	10.5	12.9
ALT OR AST > 10*ULN	10.0	0.0	5.3	6.5
ALT OR AST > 20*ULN	10.0	0.0	5.3	3.2
TOTAL BILIRUBIN (Tbili) > 2*ULN	10.0	0.0	0.0	0.0
ALP > 1.5*ULN	10.0	10.0	0.0	0.0
ALT or AST > 3xULN w/ Tbili > 1.5*ULN in 1 day	10.0	0.0	0.0	0.0
ALT or AST > 3*ULN w/ Tbili > 1.5*ULN in 30 days	10.0	0.0	0.0	0.0
ALT or AST > 3xULN w/ Tbili > 2*ULN in 1 day	10.0	0.0	0.0	0.0
ALT or AST > 3*ULN w/ Tbili > 2*ULN in 30 days	10.0	0.0	0.0	0.0

End point values	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ	Part B Cohort 1d: Arm N3+RT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	27	27	
Units: Percentage of participants				
number (not applicable)				
ALT OR AST > 3*ULN	10.0	18.5	14.8	
ALT OR AST > 5*ULN	3.3	11.1	3.7	
ALT OR AST > 10*ULN	3.3	3.7	3.7	
ALT OR AST > 20*ULN	3.3	0.0	3.7	
TOTAL BILIRUBIN (Tbili) > 2*ULN	0.0	7.4	0.0	
ALP > 1.5*ULN	3.3	0.0	3.7	
ALT or AST > 3xULN w/ Tbili > 1.5*ULN in 1 day	0.0	3.7	0.0	
ALT or AST > 3*ULN w/ Tbili > 1.5*ULN in 30 days	0.0	3.7	0.0	
ALT or AST > 3xULN w/ Tbili > 2*ULN in 1 day	0.0	3.7	0.0	
ALT or AST > 3*ULN w/ Tbili > 2*ULN in 30 days	0.0	3.7	0.0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Specific Laboratory Abnormalities in Thyroid Tests in Cohorts 1, 1b, 1c and 1d

End point title	Percentage of Participants with Specific Laboratory Abnormalities in Thyroid Tests in Cohorts 1, 1b, 1c and 1d[9][10]

End point description:

The percentage of participants who experienced a laboratory abnormality of the thyroid in each treatment arm.

MedDRA Version: 24.1

Free T3 (FT3) Free T4 (FT4) Lower Limit of Normal (LLN)

(A) Within a 2-week window after the abnormal TSH test date. (B) Includes participants with TSH abnormality and with no FT3/FT4 test values in the 2-week window or with non-abnormal value(s) from only one of the two tests and no value from the other test.

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (up to approximately 34 months).

Notes:

[9] - 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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

[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: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

End point values	Cohort 1: Arm N1+I3	Cohort 1: Arm N3	Cohort 1b: Arm N3+I1	Part A Cohort 1c: Arm N3+RT+TMZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	19	30
Units: Percentage of participants				
number (not applicable)				
TSH > ULN	20.0	50.0	10.5	23.3
TSH > ULN, WITH TSH <= ULN AT BASELINE	20.0	30.0	10.5	20.0
TSH > ULN, WITH AT LEAST ONE FT3/FT4 TEST < LLN	20.0	30.0	10.5	13.3
TSH > ULN, WITH ALL OTHER FT3/FT4 TEST >= LLN	0.0	10.0	0.0	6.7
TSH > ULN, WITH FT3/FT4 TEST MISSING	0.0	10.0	0.0	3.3
TSH < LLN	60.0	30.0	31.6	43.3
TSH < LLN, WITH TSH >= LLN AT BASELINE	60.0	30.0	31.6	33.3
TSH<LLN, LLN WITH AT LEAST ONE FT3/FT4 TEST>ULN	30.0	10.0	15.8	10.0
TSH < LLN, WITH ALL OTHER FT3/FT4 TEST <= ULN	20.0	20.0	10.5	30.0
TSH < LLN, WITH FT3/FT4 TEST MISSING	10.0	0.0	5.3	3.3

End point values	Part A Cohort	Part B Cohort	Part B Cohort	

	1d: Arm N3+RT	1c: Arm N3+RT+TMZ	1d: Arm N3+RT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	27	27	
Units: Percentage of participants				
number (not applicable)				
TSH > ULN	16.7	11.1	7.4	
TSH > ULN, WITH TSH <= ULN AT BASELINE	16.7	11.1	7.4	
TSH > ULN, WITH AT LEAST ONE FT3/FT4 TEST < LLN	13.3	7.4	0.0	
TSH > ULN, WITH ALL OTHER FT3/FT4 TEST >= LLN	0.0	3.7	7.4	
TSH > ULN, WITH FT3/FT4 TEST MISSING	3.3	0.0	0.0	
TSH < LLN	40.0	22.2	33.3	
TSH < LLN, WITH TSH >= LLN AT BASELINE	40.0	18.5	18.5	
TSH<LLN, LLN WITH AT LEAST ONE FT3/FT4 TEST>ULN	13.3	11.1	0.0	
TSH < LLN, WITH ALL OTHER FT3/FT4 TEST <= ULN	16.7	11.1	29.6	
TSH < LLN, WITH FT3/FT4 TEST MISSING	10.0	0.0	3.7	

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival (OS) for Cohort 2

End point title	Overall Survival (OS) for Cohort 2[11]

End point description:

OS was measured in months from the time of randomization to the event date (death) due to any cause. A participant who has not died will be censored at the last known alive date.

Based on Kaplan-Meier Estimates. Hazard ratio from Cox proportional hazard model stratified by presence of measurable lesions at baseline per IVRS. P-value from log-rank test stratified by presence of measurable lesions at baseline per IVRS.

End point type	Primary

End point timeframe:

Time between the date of randomization and the date of death due to any cause (up to up to 17Jun2019, approximately 5 years)

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: Prespecified to be collected for Cohort 2 only.

End point values	Cohort 2: Arm N3	Cohort 2: Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	185		
Units: Months				
median (confidence interval 95%)	9.77 (8.21 to 11.83)	10.05 (9.00 to 11.99)		

Statistical analyses

Statistical analysis title	Overall Survival (OS) Cohort 2
Comparison groups	Cohort 2: Arm N3 v Cohort 2: Arm B
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3791
Method	log-rank test stratified
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.36

Secondary: Overall Survival (OS) at 12 Months for Cohort 2	
End point title	Overall Survival (OS) at 12 Months for Cohort 2[12]
End point description:	
OS(12) is measured as the percentage of participants alive at 12 months per Kaplan-Meier curve of OS. Z test with variance estimation based on Greenwood formula using log(-log) transformation.	
End point type	Secondary
End point timeframe:	
From randomization to 12 months following randomization	

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: Prespecified to be collected for Cohort 2 only.

End point values	Cohort 2: Arm N3	Cohort 2: Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	185		
Units: Percentage of Participants				
number (confidence interval 95%)	41.8 (34.7 to 48.8)	42.4 (34.9 to 49.6)		

Statistical analyses

Statistical analysis title	Overall Survival (OS) at 12 months - Cohort 2
Comparison groups	Cohort 2: Arm N3 v Cohort 2: Arm B
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9208
Method	Z test with variance estimation based on
Parameter estimate	Difference of OS rates at 12 months
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	9.7

Secondary: Objective Response Rate (ORR) for Cohort 2

End point title	Objective Response Rate (ORR) for Cohort 2[13]

End point description:

ORR was measured by the percentage of participants whose best overall response (BOR) is confirmed Complete Response (CR) or Partial Response (PR) divided by response evaluable participants. The best overall response (BOR) is determined once all the data for the participant is known. BOR is defined as the best response designation, as determined by investigators, recorded between the date of randomization and the date of objectively documented progression per RANO criteria, the date of subsequent therapy, or date of surgical resection, whichever occurs first.

Confidence interval based on the Clopper and Pearson method. For the comparison of the odds ratio of Nivolumab over Bevacizumab, the Cochran-Mantel-Haenszel (CMH) method of weighting was utilized.

End point type	Secondary

End point timeframe:

Time from randomization to the date of the first documented tumor progression or death due to any cause (up to approximately 10 years and 5 months)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Prespecified to be collected for Cohort 2 only.

End point values	Cohort 2: Arm N3	Cohort 2: Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	156		
Units: Percentage of participants				
number (confidence interval 95%)	7.8 (4.1 to 13.3)	23.1 (16.7 to 30.5)		

Statistical analyses

Statistical analysis title	Objective Response Rate (ORR) for Cohort 2
Comparison groups	Cohort 2: Arm N3 v Cohort 2: Arm B

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Odds ratio (OR)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.59

Secondary: Overall Survival (OS) for Cohorts 1c and 1d

End point title	Overall Survival (OS) for Cohorts 1c and 1d[14]

End point description:

OS was measured in months from the time of randomization (Part B) or time of treatment (Part A) to the event date (death) due to any cause. A participant who has not died will be censored at the last known alive date.

Based on Kaplan-Meier Estimates.

End point type	Secondary

End point timeframe:

Time between the date of randomization and the date of death due to any cause (up to approximately 10 years and 5 months)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Prespecified to be collected for Cohorts 1c, and 1d only.

End point values	Part A Cohort 1c: Arm N3+RT+TMZ	Part A Cohort 1d: Arm N3+RT	Part B Cohort 1c: Arm N3+RT+TMZ	Part B Cohort 1d: Arm N3+RT
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	30	28	28
Units: Months				
median (confidence interval 95%)	22.08 (16.13 to 32.39)	14.41 (12.55 to 17.31)	15.95 (10.35 to 18.30)	13.96 (10.81 to 18.14)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) for Cohort 2

End point title	Progression Free Survival (PFS) for Cohort 2[15]

End point description:

PFS was measured in months from the time of randomization to the date of the first documented tumor progression or death due to any cause. Based on Kaplan-Meier Estimates. Hazard ratio from Cox proportional hazard model stratified by presence of measurable lesions at baseline per IVRS.

End point type	Secondary

End point timeframe:

Time from randomization to the date of the first documented tumor progression or death due to any cause (up to approximately 10 years and 5 months)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Prespecified to be collected for Cohort 2 only.

End point values	Cohort 2: Arm N3	Cohort 2: Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	185		
Units: Months				
median (confidence interval 95%)	1.51 (1.48 to 1.61)	3.61 (2.99 to 4.60)		

Statistical analyses

Statistical analysis title	Progression Free Survival (PFS) for Cohort 2
Comparison groups	Cohort 2: Arm N3 v Cohort 2: Arm B
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	2.35

Post-hoc: Post-hoc Overall Survival (OS) for Cohort 2

End point title	Post-hoc Overall Survival (OS) for Cohort 2[16]

End point description:

OS was measured in months from the time of randomization to the event date (death) due to any cause. A participant who has not died will be censored at the last known alive date.

Based on Kaplan-Meier Estimates. Hazard ratio from Cox proportional hazard model stratified by presence of measurable lesions at baseline per IVRS. P-value from log-rank test stratified by presence of measurable lesions at baseline per IVRS.

End point type	Post-hoc

End point timeframe:

Time between the date of randomization and the date of death due to any cause (up to approximately 10 years and 5 months)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Prespecified to be collected for Cohorts 1, 1b, 1c, and 1d only.

End point values	Cohort 2: Arm N3	Cohort 2: Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	185		
Units: Months				
median (confidence interval 95%)	9.77 (8.21 to 11.83)	10.05 (9.00 to 11.99)		

Statistical analyses

Statistical analysis title	Post-hoc Overall Survival (OS) for Cohort 2
Comparison groups	Cohort 2: Arm N3 v Cohort 2: Arm B
Number of subjects included in analysis	369
Analysis specification	Post-hoc
Analysis type	
P-value	= 0.3791
Method	log-rank test stratified
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.36

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and NSAEs: From first dose (SAEs and NSAEs) to 100 days post last dose (up to approximately 113 months).

Adverse event reporting additional description:

SAEs and NSAEs (Other Adverse Events) = treated participant population

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Cohort 1: Arm N3

Reporting group description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks.

Reporting group title	Cohort 1: Arm N1+I3

Reporting group description:

Nivolumab 1 mg/kg administered as a 60-minute intravenous (IV) infusion followed by ipilimumab 3 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter.

Reporting group title	Cohort 1b: Arm N3+I1

Reporting group description:

Nivolumab 3 mg/kg administered as a 60-minute IV infusion followed by ipilimumab 1 mg/kg 90-minute IV infusion every 3 weeks for 4 cycles, then nivolumab 3 mg/kg 60-minute IV every 2 weeks thereafter.

Reporting group title	Cohort 2: Arm B

Reporting group description:

Bevacizumab 10 mg/kg dosed every 2 weeks as 90-minute IV infusion for the first dose and 60-minute IV infusions for subsequent doses if the first infusion is tolerated.

Reporting group title	Part B Cohort 1c: Arm N3+RT+TMZ

Reporting group description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide.

Reporting group title	Cohort 2: Arm N3

Reporting group description:

Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks.

Reporting group title	Part B Cohort 1d: Arm N3+RT

Reporting group description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy.

Reporting group title	Part A Cohort 1c: Arm N3+RT+TMZ

Reporting group description:

Participants with newly diagnosed GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and chemoradiation followed by 6 or more cycles of maintenance temozolomide.

Reporting group title	Part A Cohort 1d: Arm N3+RT

Reporting group description:

Participants with newly diagnosed unmethylated MGMT GBM: Nivolumab 3 mg/kg dosed as 60-minute IV infusion every 2 weeks with standard of care treatment including surgical resection and radiation therapy.

Serious adverse events	Cohort 1: Arm N3	Cohort 1: Arm N1+I3	Cohort 1b: Arm N3+I1
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	8 / 10 (80.00%)	15 / 20 (75.00%)
number of deaths (all causes)	9	10	20
number of deaths resulting from adverse events	2	2	8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma multiforme			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	8 / 20 (40.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 9
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 6
Metastases to spine			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm malignant			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour flare			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flushing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 20 (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
Ischaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (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
Impaired healing			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Sudden death			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulomatous pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hiccups			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Delirium			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Agitation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Influenza B virus test positive			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (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
Lipase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Humerus fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinus tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Demyelination			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	3 / 20 (15.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemianopia homonymous			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Hemiparesis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Neurological decompensation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Slow speech			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye movement disorder			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 1	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cholecystitis acute			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis bullous			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lichen planus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
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 erythematous			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
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			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Endocrine disorders			

Autoimmune hypothyroidism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune thyroiditis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypothyroidism			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Muscular weakness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	3 / 20 (15.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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			
Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex encephalitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (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
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (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
Hypovolaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0

Serious adverse events	Cohort 2: Arm B	Part B Cohort 1c: Arm N3+RT+TMZ	Cohort 2: Arm N3
Total subjects affected by serious adverse events			
subjects affected / exposed	94 / 165 (56.97%)	16 / 28 (57.14%)	117 / 182 (64.29%)
number of deaths (all causes)	156	28	178
number of deaths resulting from adverse events	48	5	48
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenoma			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Glioblastoma multiforme			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	53 / 165 (32.12%)	4 / 28 (14.29%)	64 / 182 (35.16%)
occurrences causally related to treatment / all	0 / 55	0 / 4	0 / 66
deaths causally related to treatment / all	0 / 47	0 / 2	0 / 46
Metastases to spine			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm malignant			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour flare			
subjects affected / exposed	0 / 165 (0.00%)	3 / 28 (10.71%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			

subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Flushing			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Hypertension			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Hypotension			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	4 / 165 (2.42%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Performance status decreased			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Granulomatous pneumonitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Cough			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiccups			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Pneumothorax spontaneous			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	5 / 165 (3.03%)	0 / 28 (0.00%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Confusional state			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Delirium			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Hallucination			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Suicide attempt			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza B virus test positive			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Transaminases increased			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fracture			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hip fracture			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Infusion related reaction			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Aphasia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			

subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Demyelination			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	3 / 165 (1.82%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Headache			
subjects affected / exposed	2 / 165 (1.21%)	5 / 28 (17.86%)	10 / 182 (5.49%)
occurrences causally related to treatment / all	0 / 2	0 / 6	3 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemianopia homonymous			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Hydrocephalus			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	3 / 165 (1.82%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
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	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Presyncope			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	11 / 165 (6.67%)	4 / 28 (14.29%)	17 / 182 (9.34%)
occurrences causally related to treatment / all	0 / 12	0 / 5	4 / 25
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Slow speech			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Somnolence			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye movement disorder			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune pancreatitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Large intestine perforation			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vomiting			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Hypertransaminasaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Portal vein thrombosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Immune-mediated hepatitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Skin and subcutaneous tissue disorders			
Dermatitis bullous			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug reaction with eosinophilia and			

systemic symptoms			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Lichen planus			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
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 erythematous			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Rash maculo-papular			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
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			

Tubulointerstitial nephritis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune hypothyroidism			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune thyroiditis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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

Mobility decreased			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Encephalitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis herpes			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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
Groin abscess			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Herpes simplex encephalitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft infection			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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	2 / 165 (1.21%)	1 / 28 (3.57%)	4 / 182 (2.20%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (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 infection			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia aspiration			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Subcutaneous abscess			

subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Urinary tract infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			

subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (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
Hypomagnesaemia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B Cohort 1d: Arm N3+RT	Part A Cohort 1c: Arm N3+RT+TMZ	Part A Cohort 1d: Arm N3+RT
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 28 (67.86%)	24 / 31 (77.42%)	19 / 30 (63.33%)
number of deaths (all causes)	28	29	30
number of deaths resulting from adverse events	6	2	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colorectal adenoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma multiforme			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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 neoplasm progression			
subjects affected / exposed	7 / 28 (25.00%)	12 / 31 (38.71%)	9 / 30 (30.00%)
occurrences causally related to treatment / all	0 / 8	1 / 12	0 / 9
deaths causally related to treatment / all	0 / 4	0 / 2	0 / 6
Metastases to spine			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Neoplasm malignant			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour flare			

subjects affected / exposed	2 / 28 (7.14%)	3 / 31 (9.68%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	2 / 2	1 / 3	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flushing			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (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
Haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)	4 / 31 (12.90%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 2	3 / 4	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulomatous pneumonitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Aspiration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiccups			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 28 (3.57%)	4 / 31 (12.90%)	3 / 30 (10.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Delirium			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 1	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
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 bilirubin increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
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	0 / 28 (0.00%)	2 / 31 (6.45%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza B virus test positive			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (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
Procedural haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Demyelination			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Epilepsy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemianopia homonymous			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Hemiparesis			

subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neurological decompensation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyramidal tract syndrome			

subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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	2 / 28 (7.14%)	5 / 31 (16.13%)	4 / 30 (13.33%)
occurrences causally related to treatment / all	0 / 2	1 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Slow speech			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Thrombocytopenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Neutropenia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (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
Leukopenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye movement disorder			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune pancreatitis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Gastritis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Nausea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis bullous			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lichen planus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash erythematous			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			

subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (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
Skin ulcer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
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 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Endocrine disorders			
Autoimmune hypothyroidism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune thyroiditis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			

subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Mobility decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
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 / 28 (0.00%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neck pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Bacteraemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis herpes			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Herpes zoster			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex encephalitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Graft infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 28 (10.71%)	5 / 31 (16.13%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 4	2 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			

subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (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
Diabetes mellitus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (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
Diabetic ketoacidosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (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
Hypocalcaemia			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1: Arm N3	Cohort 1: Arm N1+I3	Cohort 1b: Arm N3+I1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 10 (100.00%)	20 / 20 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Deep vein thrombosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Pelvic venous thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	3
Oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0

Mucosal inflammation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	6 / 20 (30.00%)
occurrences (all)	2	3	6
Chills			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Face oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	5 / 10 (50.00%)	8 / 10 (80.00%)	14 / 20 (70.00%)
occurrences (all)	5	8	18
Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	2 / 20 (10.00%)
occurrences (all)	0	2	3
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	2 / 20 (10.00%)
occurrences (all)	0	2	3
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	4 / 20 (20.00%)
occurrences (all)	1	1	5
Oropharyngeal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	9 / 20 (45.00%)
occurrences (all)	2	3	11
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Dyspnoea exertional			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Tonsillar erythema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Delusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	9 / 20 (45.00%)
occurrences (all)	4	3	11

Anxiety			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Agitation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Irritability			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Hallucination			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Disorientation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	4 / 10 (40.00%)	2 / 20 (10.00%)
occurrences (all)	1	4	4
Amylase increased			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	1 / 20 (5.00%)
occurrences (all)	4	3	2
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	4 / 10 (40.00%)	3 / 20 (15.00%)
occurrences (all)	1	5	6
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Platelet count decreased			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	5
Neutrophil count decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	4
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	2 / 10 (20.00%)	4 / 10 (40.00%)	2 / 20 (10.00%)
occurrences (all)	5	6	2
White blood cell count decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
White blood cell count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Contusion			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Radiation skin injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	5 / 20 (25.00%)
occurrences (all)	0	6	13
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Myocardial infarction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Ataxia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Aphasia			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Amnesia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Disturbance in attention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	3 / 20 (15.00%)
occurrences (all)	1	1	3
Brain oedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Dysgeusia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Facial paresis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Dysarthria			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences (all)	2	1	2
Dizziness			
subjects affected / exposed	4 / 10 (40.00%)	1 / 10 (10.00%)	4 / 20 (20.00%)
occurrences (all)	4	1	4
Haemorrhage intracranial			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Dyspraxia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Memory impairment			

subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	4 / 20 (20.00%)
occurrences (all)	3	1	4
Lethargy			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	4 / 20 (20.00%)
occurrences (all)	1	0	4
Hypoaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	7 / 20 (35.00%)
occurrences (all)	3	4	7
Headache			
subjects affected / exposed	7 / 10 (70.00%)	7 / 10 (70.00%)	10 / 20 (50.00%)
occurrences (all)	12	15	11
Partial seizures			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Psychomotor skills impaired			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Vasogenic cerebral oedema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Tremor			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Seizure			

subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences (all)	2	1	2
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Visual field defect			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Vision blurred			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Optic nerve disorder			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Night blindness			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Diplopia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Anal incontinence			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	3 / 20 (15.00%)
occurrences (all)	1	0	3
Vomiting			
subjects affected / exposed	2 / 10 (20.00%)	4 / 10 (40.00%)	4 / 20 (20.00%)
occurrences (all)	2	9	4
Toothache			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Constipation			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	4 / 20 (20.00%)
occurrences (all)	3	0	4
Dysphagia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)	7 / 10 (70.00%)	7 / 20 (35.00%)
occurrences (all)	2	13	12
Cheilitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	6 / 20 (30.00%)
occurrences (all)	4	6	8
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	6 / 20 (30.00%)
occurrences (all)	2	0	7
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	1 / 20 (5.00%)
occurrences (all)	0	3	1
Drug eruption			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Alopecia			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)	4 / 10 (40.00%)	2 / 20 (10.00%)
occurrences (all)	0	5	2
Rash			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	5 / 20 (25.00%)
occurrences (all)	2	1	6
Renal and urinary disorders			
Urinary hesitation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	4 / 20 (20.00%)
occurrences (all)	0	1	4
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Endocrine disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cushingoid			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Hypothyroidism			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	2	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	3 / 20 (15.00%)
occurrences (all)	2	0	3
Groin pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	3 / 10 (30.00%)	2 / 10 (20.00%)	5 / 20 (25.00%)
occurrences (all)	3	2	6
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Spinal pain			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Scoliosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Infections and infestations			
Mucosal infection			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Klebsiella infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Candida infection			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	2 / 20 (10.00%)
occurrences (all)	0	2	3
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	4	0	0
Oral candidiasis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	1	1	2
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Rash pustular			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Staphylococcal infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	5 / 20 (25.00%)
occurrences (all)	0	0	5
Viral infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	3 / 20 (15.00%)
occurrences (all)	0	4	3
Dehydration			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences (all)	1	1	3
Hyperglycaemia			
subjects affected / exposed	3 / 10 (30.00%)	0 / 10 (0.00%)	5 / 20 (25.00%)
occurrences (all)	3	0	8
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperlipasaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	4
Hypomagnesaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	2
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	2 / 20 (10.00%)
occurrences (all)	0	1	3

Non-serious adverse events	Cohort 2: Arm B	Part B Cohort 1c: Arm N3+RT+TMZ	Cohort 2: Arm N3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	148 / 165 (89.70%)	27 / 28 (96.43%)	168 / 182 (92.31%)
Vascular disorders			
Hypotension			

subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences (all)	2	1	3
Hypertension			
subjects affected / exposed	50 / 165 (30.30%)	3 / 28 (10.71%)	12 / 182 (6.59%)
occurrences (all)	63	3	18
Deep vein thrombosis			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	2	1	2
Pelvic venous thrombosis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	0	0	2
Asthenia			
subjects affected / exposed	9 / 165 (5.45%)	3 / 28 (10.71%)	14 / 182 (7.69%)
occurrences (all)	11	3	15
Oedema			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	4 / 165 (2.42%)	3 / 28 (10.71%)	1 / 182 (0.55%)
occurrences (all)	5	3	1
Mucosal inflammation			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	2	2	2
Influenza like illness			
subjects affected / exposed	5 / 165 (3.03%)	2 / 28 (7.14%)	2 / 182 (1.10%)
occurrences (all)	5	2	2
Gait disturbance			
subjects affected / exposed	7 / 165 (4.24%)	2 / 28 (7.14%)	16 / 182 (8.79%)
occurrences (all)	7	2	18
Chills			

subjects affected / exposed	2 / 165 (1.21%)	2 / 28 (7.14%)	3 / 182 (1.65%)
occurrences (all)	2	2	3
Face oedema			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences (all)	0	2	1
Fatigue			
subjects affected / exposed	45 / 165 (27.27%)	20 / 28 (71.43%)	69 / 182 (37.91%)
occurrences (all)	56	24	84
Pain			
subjects affected / exposed	5 / 165 (3.03%)	5 / 28 (17.86%)	4 / 182 (2.20%)
occurrences (all)	5	5	4
Oedema peripheral			
subjects affected / exposed	15 / 165 (9.09%)	0 / 28 (0.00%)	16 / 182 (8.79%)
occurrences (all)	15	0	18
Pyrexia			
subjects affected / exposed	8 / 165 (4.85%)	3 / 28 (10.71%)	13 / 182 (7.14%)
occurrences (all)	9	3	21
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	10 / 165 (6.06%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	11	0	2
Nasal congestion			
subjects affected / exposed	3 / 165 (1.82%)	2 / 28 (7.14%)	7 / 182 (3.85%)
occurrences (all)	3	2	7
Oropharyngeal pain			
subjects affected / exposed	7 / 165 (4.24%)	3 / 28 (10.71%)	7 / 182 (3.85%)
occurrences (all)	7	4	9
Pneumonitis			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	3 / 182 (1.65%)
occurrences (all)	2	0	3
Cough			

subjects affected / exposed	12 / 165 (7.27%)	3 / 28 (10.71%)	23 / 182 (12.64%)
occurrences (all)	13	4	26
Dysphonia			
subjects affected / exposed	10 / 165 (6.06%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	10	0	3
Dyspnoea			
subjects affected / exposed	9 / 165 (5.45%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences (all)	10	1	5
Dyspnoea exertional			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	2	0	1
Tonsillar erythema			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	4 / 165 (2.42%)	2 / 28 (7.14%)	5 / 182 (2.75%)
occurrences (all)	4	2	5
Psychiatric disorders			
Depression			
subjects affected / exposed	10 / 165 (6.06%)	6 / 28 (21.43%)	6 / 182 (3.30%)
occurrences (all)	10	6	6
Delusion			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	10 / 165 (6.06%)	6 / 28 (21.43%)	15 / 182 (8.24%)
occurrences (all)	10	6	15
Anxiety			
subjects affected / exposed	6 / 165 (3.64%)	1 / 28 (3.57%)	6 / 182 (3.30%)
occurrences (all)	6	1	6
Agitation			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences (all)	0	0	5
Irritability			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	2	0	2

Insomnia			
subjects affected / exposed	15 / 165 (9.09%)	6 / 28 (21.43%)	16 / 182 (8.79%)
occurrences (all)	15	7	18
Hallucination			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	0	0	1
Disorientation			
subjects affected / exposed	3 / 165 (1.82%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	3	0	3
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	5 / 182 (2.75%)
occurrences (all)	0	2	5
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 165 (1.82%)	4 / 28 (14.29%)	6 / 182 (3.30%)
occurrences (all)	4	4	7
Amylase increased			
subjects affected / exposed	3 / 165 (1.82%)	2 / 28 (7.14%)	4 / 182 (2.20%)
occurrences (all)	3	3	4
Alanine aminotransferase increased			
subjects affected / exposed	10 / 165 (6.06%)	5 / 28 (17.86%)	16 / 182 (8.79%)
occurrences (all)	12	5	19
Weight decreased			
subjects affected / exposed	7 / 165 (4.24%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences (all)	7	1	5
Platelet count decreased			
subjects affected / exposed	5 / 165 (3.03%)	5 / 28 (17.86%)	7 / 182 (3.85%)
occurrences (all)	5	7	8
Neutrophil count decreased			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	2	1	0
Lymphocyte count decreased			
subjects affected / exposed	5 / 165 (3.03%)	3 / 28 (10.71%)	2 / 182 (1.10%)
occurrences (all)	5	8	5
Weight increased			

subjects affected / exposed	4 / 165 (2.42%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences (all)	4	1	5
Blood thyroid stimulating hormone increased			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	3 / 182 (1.65%)
occurrences (all)	2	0	3
Blood creatinine increased			
subjects affected / exposed	2 / 165 (1.21%)	3 / 28 (10.71%)	3 / 182 (1.65%)
occurrences (all)	2	3	4
Blood bilirubin increased			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences (all)	1	1	3
Lipase increased			
subjects affected / exposed	5 / 165 (3.03%)	2 / 28 (7.14%)	10 / 182 (5.49%)
occurrences (all)	6	2	15
White blood cell count decreased			
subjects affected / exposed	3 / 165 (1.82%)	2 / 28 (7.14%)	2 / 182 (1.10%)
occurrences (all)	3	4	2
White blood cell count increased			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 165 (0.61%)	2 / 28 (7.14%)	4 / 182 (2.20%)
occurrences (all)	1	2	5
Vaccination complication			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Radiation skin injury			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	0 / 182 (0.00%)
occurrences (all)	0	2	0
Infusion related reaction			

subjects affected / exposed	1 / 165 (0.61%)	2 / 28 (7.14%)	3 / 182 (1.65%)
occurrences (all)	1	2	4
Fall			
subjects affected / exposed	10 / 165 (6.06%)	2 / 28 (7.14%)	18 / 182 (9.89%)
occurrences (all)	14	2	33
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences (all)	2	1	1
Palpitations			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	1	0	0
Myocardial infarction			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 165 (0.00%)	3 / 28 (10.71%)	7 / 182 (3.85%)
occurrences (all)	0	3	9
Ataxia			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences (all)	2	0	5
Aphasia			
subjects affected / exposed	21 / 165 (12.73%)	5 / 28 (17.86%)	28 / 182 (15.38%)
occurrences (all)	22	5	31
Amnesia			
subjects affected / exposed	3 / 165 (1.82%)	0 / 28 (0.00%)	4 / 182 (2.20%)
occurrences (all)	3	0	4
Disturbance in attention			
subjects affected / exposed	2 / 165 (1.21%)	3 / 28 (10.71%)	9 / 182 (4.95%)
occurrences (all)	2	3	9
Cognitive disorder			

subjects affected / exposed	6 / 165 (3.64%)	1 / 28 (3.57%)	10 / 182 (5.49%)
occurrences (all)	6	1	13
Brain oedema			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	8 / 182 (4.40%)
occurrences (all)	0	2	8
Dysgeusia			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	1 / 182 (0.55%)
occurrences (all)	0	2	1
Facial paresis			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences (all)	2	1	1
Dysarthria			
subjects affected / exposed	5 / 165 (3.03%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences (all)	5	0	6
Dizziness			
subjects affected / exposed	11 / 165 (6.67%)	2 / 28 (7.14%)	16 / 182 (8.79%)
occurrences (all)	17	2	18
Haemorrhage intracranial			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	1	0	1
Dyspraxia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	5 / 165 (3.03%)	3 / 28 (10.71%)	9 / 182 (4.95%)
occurrences (all)	5	3	11
Memory impairment			
subjects affected / exposed	10 / 165 (6.06%)	1 / 28 (3.57%)	14 / 182 (7.69%)
occurrences (all)	10	1	17
Lethargy			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	1	0	1
Hypoaesthesia			
subjects affected / exposed	5 / 165 (3.03%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences (all)	5	1	6
Hemiparesis			

subjects affected / exposed	16 / 165 (9.70%)	4 / 28 (14.29%)	27 / 182 (14.84%)
occurrences (all)	18	4	29
Headache			
subjects affected / exposed	53 / 165 (32.12%)	17 / 28 (60.71%)	57 / 182 (31.32%)
occurrences (all)	85	23	91
Partial seizures			
subjects affected / exposed	4 / 165 (2.42%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences (all)	6	0	5
Presyncope			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	1	0	2
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	3 / 182 (1.65%)
occurrences (all)	1	0	4
Psychomotor skills impaired			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	2	1	2
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	4 / 165 (2.42%)	1 / 28 (3.57%)	4 / 182 (2.20%)
occurrences (all)	4	1	5
Syncope			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	1	0	1
Seizure			
subjects affected / exposed	17 / 165 (10.30%)	6 / 28 (21.43%)	33 / 182 (18.13%)
occurrences (all)	22	7	68
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	4 / 165 (2.42%)	2 / 28 (7.14%)	8 / 182 (4.40%)
occurrences (all)	4	2	16

Lymphopenia			
subjects affected / exposed	4 / 165 (2.42%)	2 / 28 (7.14%)	6 / 182 (3.30%)
occurrences (all)	4	2	6
Thrombocytopenia			
subjects affected / exposed	3 / 165 (1.82%)	5 / 28 (17.86%)	2 / 182 (1.10%)
occurrences (all)	3	6	2
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	3 / 165 (1.82%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences (all)	3	2	3
Tinnitus			
subjects affected / exposed	1 / 165 (0.61%)	2 / 28 (7.14%)	1 / 182 (0.55%)
occurrences (all)	1	2	1
Eye disorders			
Visual field defect			
subjects affected / exposed	3 / 165 (1.82%)	2 / 28 (7.14%)	3 / 182 (1.65%)
occurrences (all)	3	2	3
Vision blurred			
subjects affected / exposed	4 / 165 (2.42%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences (all)	5	1	5
Optic nerve disorder			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Night blindness			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	2 / 182 (1.10%)
occurrences (all)	0	2	2
Dry eye			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	0	1	2
Diplopia			

subjects affected / exposed	1 / 165 (0.61%)	2 / 28 (7.14%)	1 / 182 (0.55%)
occurrences (all)	1	2	1
Blepharitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	4 / 182 (2.20%)
occurrences (all)	0	2	4
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	0 / 182 (0.00%)
occurrences (all)	0	2	0
Anal incontinence			
subjects affected / exposed	1 / 165 (0.61%)	2 / 28 (7.14%)	4 / 182 (2.20%)
occurrences (all)	1	2	4
Abdominal pain			
subjects affected / exposed	5 / 165 (3.03%)	2 / 28 (7.14%)	17 / 182 (9.34%)
occurrences (all)	7	2	19
Vomiting			
subjects affected / exposed	11 / 165 (6.67%)	7 / 28 (25.00%)	15 / 182 (8.24%)
occurrences (all)	12	8	19
Toothache			
subjects affected / exposed	4 / 165 (2.42%)	0 / 28 (0.00%)	4 / 182 (2.20%)
occurrences (all)	4	0	4
Stomatitis			
subjects affected / exposed	6 / 165 (3.64%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	7	2	2
Constipation			
subjects affected / exposed	15 / 165 (9.09%)	12 / 28 (42.86%)	26 / 182 (14.29%)
occurrences (all)	17	14	29
Dysphagia			
subjects affected / exposed	4 / 165 (2.42%)	1 / 28 (3.57%)	5 / 182 (2.75%)
occurrences (all)	4	1	6
Dyspepsia			
subjects affected / exposed	5 / 165 (3.03%)	0 / 28 (0.00%)	9 / 182 (4.95%)
occurrences (all)	5	0	10

Diarrhoea			
subjects affected / exposed	16 / 165 (9.70%)	3 / 28 (10.71%)	28 / 182 (15.38%)
occurrences (all)	24	4	39
Cheilitis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	22 / 165 (13.33%)	15 / 28 (53.57%)	27 / 182 (14.84%)
occurrences (all)	28	20	40
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 165 (4.24%)	2 / 28 (7.14%)	20 / 182 (10.99%)
occurrences (all)	9	3	27
Erythema			
subjects affected / exposed	4 / 165 (2.42%)	0 / 28 (0.00%)	4 / 182 (2.20%)
occurrences (all)	4	0	4
Dry skin			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	13 / 182 (7.14%)
occurrences (all)	2	0	14
Drug eruption			
subjects affected / exposed	0 / 165 (0.00%)	2 / 28 (7.14%)	0 / 182 (0.00%)
occurrences (all)	0	3	0
Dermatitis contact			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 165 (0.61%)	4 / 28 (14.29%)	1 / 182 (0.55%)
occurrences (all)	1	4	1
Dermatitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	1	0	2
Dermatitis acneiform			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences (all)	1	1	5
Rash maculo-papular			

subjects affected / exposed	3 / 165 (1.82%)	1 / 28 (3.57%)	7 / 182 (3.85%)
occurrences (all)	3	1	10
Rash			
subjects affected / exposed	8 / 165 (4.85%)	2 / 28 (7.14%)	18 / 182 (9.89%)
occurrences (all)	9	2	27
Renal and urinary disorders			
Urinary hesitation			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	12 / 165 (7.27%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	18	0	0
Pollakiuria			
subjects affected / exposed	3 / 165 (1.82%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	3	1	3
Micturition urgency			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	1	1	0
Urinary incontinence			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	8 / 182 (4.40%)
occurrences (all)	2	1	8
Acute kidney injury			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	0	0	2
Urinary retention			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	1	0	2
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences (all)	0	0	5
Endocrine disorder			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Cushingoid			

subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	2	0	2
Hypothyroidism			
subjects affected / exposed	2 / 165 (1.21%)	2 / 28 (7.14%)	9 / 182 (4.95%)
occurrences (all)	2	2	9
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	11 / 165 (6.67%)	1 / 28 (3.57%)	13 / 182 (7.14%)
occurrences (all)	12	1	14
Arthralgia			
subjects affected / exposed	22 / 165 (13.33%)	7 / 28 (25.00%)	26 / 182 (14.29%)
occurrences (all)	24	7	29
Groin pain			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	15 / 165 (9.09%)	3 / 28 (10.71%)	15 / 182 (8.24%)
occurrences (all)	15	4	17
Muscle spasms			
subjects affected / exposed	5 / 165 (3.03%)	0 / 28 (0.00%)	10 / 182 (5.49%)
occurrences (all)	5	0	13
Flank pain			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	9 / 165 (5.45%)	0 / 28 (0.00%)	15 / 182 (8.24%)
occurrences (all)	9	0	18
Spinal pain			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Scoliosis			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			

subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	6 / 165 (3.64%)	1 / 28 (3.57%)	6 / 182 (3.30%)
occurrences (all)	7	1	6
Myalgia			
subjects affected / exposed	10 / 165 (6.06%)	3 / 28 (10.71%)	7 / 182 (3.85%)
occurrences (all)	11	4	7
Infections and infestations			
Mucosal infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	0	1	0
Klebsiella infection			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	0 / 182 (0.00%)
occurrences (all)	0	3	0
Enterocolitis infectious			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	1	0	0
Candida infection			
subjects affected / exposed	4 / 165 (2.42%)	2 / 28 (7.14%)	1 / 182 (0.55%)
occurrences (all)	4	2	1
Herpes zoster			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	6 / 165 (3.64%)	1 / 28 (3.57%)	7 / 182 (3.85%)
occurrences (all)	7	1	8
Oral candidiasis			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences (all)	2	1	3

Pneumonia			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	5 / 182 (2.75%)
occurrences (all)	2	0	5
Rash pustular			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	2 / 165 (1.21%)	1 / 28 (3.57%)	3 / 182 (1.65%)
occurrences (all)	3	1	4
Staphylococcal infection			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 165 (3.64%)	1 / 28 (3.57%)	6 / 182 (3.30%)
occurrences (all)	6	1	8
Urinary tract infection			
subjects affected / exposed	7 / 165 (4.24%)	1 / 28 (3.57%)	11 / 182 (6.04%)
occurrences (all)	7	1	18
Viral infection			
subjects affected / exposed	3 / 165 (1.82%)	0 / 28 (0.00%)	1 / 182 (0.55%)
occurrences (all)	4	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 165 (5.45%)	7 / 28 (25.00%)	11 / 182 (6.04%)
occurrences (all)	9	7	12
Dehydration			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	3 / 182 (1.65%)
occurrences (all)	2	0	8
Hyperglycaemia			
subjects affected / exposed	4 / 165 (2.42%)	6 / 28 (21.43%)	10 / 182 (5.49%)
occurrences (all)	5	10	14
Hyperkalaemia			

subjects affected / exposed	2 / 165 (1.21%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	5	0	2
Hyperlipasaemia			
subjects affected / exposed	0 / 165 (0.00%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	0 / 182 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 28 (3.57%)	2 / 182 (1.10%)
occurrences (all)	0	1	2
Hyponatraemia			
subjects affected / exposed	1 / 165 (0.61%)	2 / 28 (7.14%)	4 / 182 (2.20%)
occurrences (all)	1	3	4
Hypomagnesaemia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 28 (0.00%)	2 / 182 (1.10%)
occurrences (all)	1	0	2
Hypocalcaemia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 28 (3.57%)	1 / 182 (0.55%)
occurrences (all)	1	2	6
Hypokalaemia			
subjects affected / exposed	6 / 165 (3.64%)	2 / 28 (7.14%)	5 / 182 (2.75%)
occurrences (all)	10	3	42

Non-serious adverse events	Part B Cohort 1d: Arm N3+RT	Part A Cohort 1c: Arm N3+RT+TMZ	Part A Cohort 1d: Arm N3+RT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)	31 / 31 (100.00%)	29 / 30 (96.67%)
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Hypertension			
subjects affected / exposed	1 / 28 (3.57%)	5 / 31 (16.13%)	6 / 30 (20.00%)
occurrences (all)	1	7	6
Deep vein thrombosis			

subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Pelvic venous thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	1	1	1
Oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	1	1	1
Mucosal inflammation			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Influenza like illness			
subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	3	0	0
Gait disturbance			
subjects affected / exposed	0 / 28 (0.00%)	5 / 31 (16.13%)	3 / 30 (10.00%)
occurrences (all)	0	5	3
Chills			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	2 / 30 (6.67%)
occurrences (all)	2	2	2
Face oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	18 / 28 (64.29%)	25 / 31 (80.65%)	16 / 30 (53.33%)
occurrences (all)	19	29	19
Pain			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Oedema peripheral			
subjects affected / exposed	2 / 28 (7.14%)	4 / 31 (12.90%)	2 / 30 (6.67%)
occurrences (all)	2	5	2
Pyrexia			
subjects affected / exposed	6 / 28 (21.43%)	3 / 31 (9.68%)	3 / 30 (10.00%)
occurrences (all)	6	3	5
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	3 / 28 (10.71%)	4 / 31 (12.90%)	2 / 30 (6.67%)
occurrences (all)	3	5	2
Oropharyngeal pain			
subjects affected / exposed	0 / 28 (0.00%)	3 / 31 (9.68%)	0 / 30 (0.00%)
occurrences (all)	0	3	0
Pneumonitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	5 / 28 (17.86%)	5 / 31 (16.13%)	5 / 30 (16.67%)
occurrences (all)	6	6	5
Dysphonia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			

subjects affected / exposed	2 / 28 (7.14%)	3 / 31 (9.68%)	1 / 30 (3.33%)
occurrences (all)	2	3	1
Dyspnoea exertional			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tonsillar erythema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	3 / 30 (10.00%)
occurrences (all)	1	1	3
Delusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	3 / 28 (10.71%)	2 / 31 (6.45%)	3 / 30 (10.00%)
occurrences (all)	4	4	6
Anxiety			
subjects affected / exposed	4 / 28 (14.29%)	4 / 31 (12.90%)	5 / 30 (16.67%)
occurrences (all)	4	4	5
Agitation			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Irritability			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	3 / 28 (10.71%)	2 / 31 (6.45%)	5 / 30 (16.67%)
occurrences (all)	3	2	5
Hallucination			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Disorientation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)	9 / 31 (29.03%)	3 / 30 (10.00%)
occurrences (all)	2	19	5
Amylase increased			
subjects affected / exposed	2 / 28 (7.14%)	4 / 31 (12.90%)	2 / 30 (6.67%)
occurrences (all)	4	10	3
Alanine aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)	9 / 31 (29.03%)	5 / 30 (16.67%)
occurrences (all)	3	17	7
Weight decreased			
subjects affected / exposed	3 / 28 (10.71%)	4 / 31 (12.90%)	3 / 30 (10.00%)
occurrences (all)	3	5	3
Platelet count decreased			
subjects affected / exposed	2 / 28 (7.14%)	8 / 31 (25.81%)	2 / 30 (6.67%)
occurrences (all)	2	27	2
Neutrophil count decreased			
subjects affected / exposed	0 / 28 (0.00%)	5 / 31 (16.13%)	0 / 30 (0.00%)
occurrences (all)	0	28	0
Lymphocyte count decreased			
subjects affected / exposed	2 / 28 (7.14%)	6 / 31 (19.35%)	3 / 30 (10.00%)
occurrences (all)	2	14	3
Weight increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			

subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	3
Blood bilirubin increased			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	2 / 30 (6.67%)
occurrences (all)	0	5	2
Lipase increased			
subjects affected / exposed	1 / 28 (3.57%)	6 / 31 (19.35%)	5 / 30 (16.67%)
occurrences (all)	2	15	6
White blood cell count decreased			
subjects affected / exposed	1 / 28 (3.57%)	6 / 31 (19.35%)	1 / 30 (3.33%)
occurrences (all)	1	25	1
White blood cell count increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Vaccination complication			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Radiation skin injury			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	1	1	1
Infusion related reaction			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 28 (3.57%)	3 / 31 (9.68%)	3 / 30 (10.00%)
occurrences (all)	2	5	3
Cardiac disorders			

Sinus tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Myocardial infarction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Aphasia			
subjects affected / exposed	3 / 28 (10.71%)	6 / 31 (19.35%)	3 / 30 (10.00%)
occurrences (all)	3	6	3
Amnesia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Disturbance in attention			
subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Cognitive disorder			
subjects affected / exposed	3 / 28 (10.71%)	5 / 31 (16.13%)	2 / 30 (6.67%)
occurrences (all)	3	5	2
Brain oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			

subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	2 / 30 (6.67%)
occurrences (all)	1	3	2
Facial paresis			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Dysarthria			
subjects affected / exposed	4 / 28 (14.29%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences (all)	4	2	1
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	8 / 31 (25.81%)	5 / 30 (16.67%)
occurrences (all)	3	8	7
Haemorrhage intracranial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dyspraxia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	2 / 28 (7.14%)	3 / 31 (9.68%)	1 / 30 (3.33%)
occurrences (all)	2	3	1
Memory impairment			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	3 / 30 (10.00%)
occurrences (all)	1	2	3
Lethargy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	5 / 30 (16.67%)
occurrences (all)	1	2	5
Hemiparesis			
subjects affected / exposed	3 / 28 (10.71%)	5 / 31 (16.13%)	2 / 30 (6.67%)
occurrences (all)	3	5	2
Headache			
subjects affected / exposed	11 / 28 (39.29%)	14 / 31 (45.16%)	13 / 30 (43.33%)
occurrences (all)	14	25	16
Partial seizures			

subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Presyncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Psychomotor skills impaired			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Vasogenic cerebral oedema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	2 / 28 (7.14%)	2 / 31 (6.45%)	3 / 30 (10.00%)
occurrences (all)	2	2	3
Syncope			
subjects affected / exposed	0 / 28 (0.00%)	3 / 31 (9.68%)	0 / 30 (0.00%)
occurrences (all)	0	3	0
Seizure			
subjects affected / exposed	12 / 28 (42.86%)	3 / 31 (9.68%)	7 / 30 (23.33%)
occurrences (all)	18	9	8
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	4 / 28 (14.29%)	7 / 31 (22.58%)	1 / 30 (3.33%)
occurrences (all)	6	11	1
Lymphopenia			
subjects affected / exposed	0 / 28 (0.00%)	3 / 31 (9.68%)	1 / 30 (3.33%)
occurrences (all)	0	5	2
Thrombocytopenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	2 / 30 (6.67%)
occurrences (all)	1	1	2
Vertigo			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Tinnitus			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Eye disorders			
Visual field defect			
subjects affected / exposed	0 / 28 (0.00%)	3 / 31 (9.68%)	0 / 30 (0.00%)
occurrences (all)	0	3	0
Vision blurred			
subjects affected / exposed	0 / 28 (0.00%)	6 / 31 (19.35%)	3 / 30 (10.00%)
occurrences (all)	0	6	3
Optic nerve disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Night blindness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	2 / 28 (7.14%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences (all)	2	2	1
Diplopia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Visual impairment			

subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	3 / 28 (10.71%)	4 / 31 (12.90%)	3 / 30 (10.00%)
occurrences (all)	3	9	3
Vomiting			
subjects affected / exposed	3 / 28 (10.71%)	6 / 31 (19.35%)	3 / 30 (10.00%)
occurrences (all)	5	15	3
Toothache			
subjects affected / exposed	1 / 28 (3.57%)	3 / 31 (9.68%)	0 / 30 (0.00%)
occurrences (all)	1	4	0
Stomatitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 31 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	1
Constipation			
subjects affected / exposed	1 / 28 (3.57%)	10 / 31 (32.26%)	4 / 30 (13.33%)
occurrences (all)	2	11	4
Dysphagia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	2 / 30 (6.67%)
occurrences (all)	2	1	2
Dyspepsia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	2 / 30 (6.67%)
occurrences (all)	0	2	2
Diarrhoea			
subjects affected / exposed	8 / 28 (28.57%)	8 / 31 (25.81%)	4 / 30 (13.33%)
occurrences (all)	11	20	5
Cheilitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Nausea			
subjects affected / exposed	7 / 28 (25.00%)	13 / 31 (41.94%)	8 / 30 (26.67%)
occurrences (all)	7	24	10
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 28 (14.29%)	7 / 31 (22.58%)	3 / 30 (10.00%)
occurrences (all)	4	9	3
Erythema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	3 / 28 (10.71%)	8 / 31 (25.81%)	1 / 30 (3.33%)
occurrences (all)	3	8	1
Drug eruption			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	5 / 28 (17.86%)	6 / 31 (19.35%)	2 / 30 (6.67%)
occurrences (all)	5	7	2
Dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Rash maculo-papular			
subjects affected / exposed	1 / 28 (3.57%)	5 / 31 (16.13%)	4 / 30 (13.33%)
occurrences (all)	1	5	4
Rash			
subjects affected / exposed	9 / 28 (32.14%)	8 / 31 (25.81%)	2 / 30 (6.67%)
occurrences (all)	9	12	3
Renal and urinary disorders			

Urinary hesitation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	3	1	0
Micturition urgency			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Urinary incontinence			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	3 / 30 (10.00%)
occurrences (all)	1	1	3
Acute kidney injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Urinary retention			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	3 / 30 (10.00%)
occurrences (all)	0	2	3
Endocrine disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Cushingoid			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	3 / 28 (10.71%)	3 / 31 (9.68%)	3 / 30 (10.00%)
occurrences (all)	3	4	3
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	5 / 28 (17.86%)	6 / 31 (19.35%)	2 / 30 (6.67%)
occurrences (all)	5	7	2
Arthralgia			
subjects affected / exposed	4 / 28 (14.29%)	9 / 31 (29.03%)	4 / 30 (13.33%)
occurrences (all)	4	10	4
Groin pain			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Muscular weakness			
subjects affected / exposed	3 / 28 (10.71%)	3 / 31 (9.68%)	2 / 30 (6.67%)
occurrences (all)	3	3	2
Muscle spasms			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	1	1	1
Flank pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	3 / 30 (10.00%)
occurrences (all)	0	1	3
Spinal pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Scoliosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 31 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Myalgia			
subjects affected / exposed	0 / 28 (0.00%)	3 / 31 (9.68%)	1 / 30 (3.33%)
occurrences (all)	0	4	1

Infections and infestations			
Mucosal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Klebsiella infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	1	4	0
Enterocolitis infectious			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	3 / 28 (10.71%)	1 / 31 (3.23%)	3 / 30 (10.00%)
occurrences (all)	3	1	4
Herpes zoster			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	1 / 30 (3.33%)
occurrences (all)	0	4	1
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	3 / 28 (10.71%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	3	1	1
Pneumonia			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Rash pustular			
subjects affected / exposed	1 / 28 (3.57%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Sinusitis			

subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Staphylococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 31 (3.23%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	4 / 31 (12.90%)	1 / 30 (3.33%)
occurrences (all)	1	5	1
Urinary tract infection			
subjects affected / exposed	2 / 28 (7.14%)	1 / 31 (3.23%)	2 / 30 (6.67%)
occurrences (all)	2	2	2
Viral infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 28 (32.14%)	5 / 31 (16.13%)	3 / 30 (10.00%)
occurrences (all)	10	7	3
Dehydration			
subjects affected / exposed	4 / 28 (14.29%)	3 / 31 (9.68%)	1 / 30 (3.33%)
occurrences (all)	5	3	1
Hyperglycaemia			
subjects affected / exposed	2 / 28 (7.14%)	7 / 31 (22.58%)	7 / 30 (23.33%)
occurrences (all)	3	28	9
Hyperkalaemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Hyperlipasaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 31 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	0	2	0

Hypoalbuminaemia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	2 / 28 (7.14%)	5 / 31 (16.13%)	5 / 30 (16.67%)
occurrences (all)	3	7	5
Hypomagnesaemia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 31 (6.45%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Hypocalcaemia			
subjects affected / exposed	1 / 28 (3.57%)	3 / 31 (9.68%)	1 / 30 (3.33%)
occurrences (all)	1	3	1
Hypokalaemia			
subjects affected / exposed	2 / 28 (7.14%)	4 / 31 (12.90%)	2 / 30 (6.67%)
occurrences (all)	2	7	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2013	Adds 12-lead ECG at screening and as clinically indicated while on treatment; Clarifies guidance regarding corticosteroid use during the study; Includes guidance on the use of PPI or H2 blockers for patients on chronic steroids; Excludes patients with a history of gastrointestinal diverticulitis. Corrects inconsistencies in the statistical considerations section
15 July 2014	Updated title of protocol Added selection of dose and study design for Cohort 2:Since evaluation of a second dosing regimen for the combination therapy is on-going, the randomized portion of this study (Cohort 2) will be limited to nivolumab monotherapy versus bevacizumab randomized in a 1:1 ratio. Study design, rationale for dose selection, study hypothesis, study objectives, and statistical considerations updated accordingly. Added details for Cohort 1b (US sites only) Clarified inclusion that required a measurable lesion at baseline is limited to Cohort 1 and 1b; Clarified the interval of time after surgical resection to be 28days for inclusion; Clarified interval of time for baseline MRI to be 21 days instead of 28 days Clarified exclusion of active, known or suspected autoimmune disease
27 February 2015	Increase sample size of Cohort by 120 subjects to 340 Change from 2plannedinterim analyses to a single interim analysis at 80% of the total number of events Added clarification to allow collection of OS data outside the protocol specified windows
15 August 2015	Added Cogstate assessment to Cohort 2 Added clarification for allowing resection for assessment of progression/pseudoprogression. Added central neruopathic review of tumor samples obtained after biopsy or resection in subjects for whom determination of progression versus pseudoprogression cannot be determined Changed confirmation of progression to be 12 weeks rather than 8 weeks after initial radiologic progression for subjects who meet criteria for continuation of study treatment. Added table to summarize assessment of best overall response (BOR). Combined site specific amendment for Cohort1b into global protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported