



Clinical trial results:

A Phase 2 Study of Nivolumab in Combination with Either Rucaparib, Docetaxel, or Enzalutamide in Men with Castration-resistant Metastatic Prostate Cancer (CheckMate 9KD: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 9KD)

Summary

EudraCT number	2017-001626-17
Trial protocol	DE ES FR
Global end of trial date	10 January 2025

Results information

Result version number	v1 (current)
This version publication date	24 January 2026
First version publication date	24 January 2026

Trial information

Trial identification

Sponsor protocol code	CA209-9KD
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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	Chausse de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, 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	06 February 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate efficacy of nivolumab combined with either rucaparib, docetaxel, or enzalutamide in participants with Castration-resistant Metastatic Prostate Cancer

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 17
Country: Number of subjects enrolled	Australia: 24
Country: Number of subjects enrolled	Brazil: 38
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Chile: 16
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Mexico: 19
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	United States: 72
Worldwide total number of subjects	292
EEA total number of subjects	90

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	95
From 65 to 84 years	192
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

292 participants treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Arm A1
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Arm description:

Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have at least 1 but no more than 2 prior chemotherapy regimens

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg every four weeks

Arm title	Arm A2
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Arm description:

Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have not received prior chemotherapy regimen

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg every four weeks

Arm title	Arm B
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Arm description:

Nivolumab 360 mg IV Q3W + Docetaxel 75 mg/m² IV Q3W + Prednisone 5 mg PO BID

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

360 mg every three weeks

Arm title	Arm C
Arm description:	
Nivolumab 480 mg IV Q4W + Enzalutamide 160 mg PO QD	
Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
480 mg every four weeks	

Number of subjects in period 1	Arm A1	Arm A2	Arm B
Started	88	71	84
Completed	0	3	1
Not completed	88	68	83
Adverse event, serious fatal	2	1	1
Participant withdrew consent	1	-	1
Maximum clinical benefit	-	-	1
Participant no longer meets study criteria	-	-	1
Adverse Event unrelated to Study Drug	4	4	6
Other reasons	-	5	1
Study Drug Toxicity	12	8	14
Poor/non-compliance	-	1	-
Disease Progression	65	46	54
Participant request to discontinue study treatment	4	3	3
Administrative reason by sponsor	-	-	1

Number of subjects in period 1	Arm C
Started	49
Completed	0
Not completed	49
Adverse event, serious fatal	-
Participant withdrew consent	1
Maximum clinical benefit	-
Participant no longer meets study criteria	-
Adverse Event unrelated to Study Drug	4
Other reasons	1
Study Drug Toxicity	-

Poor/non-compliance	-
Disease Progression	42
Participant request to discontinue study treatment	1
Administrative reason by sponsor	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A1
Reporting group description: Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have at least 1 but no more than 2 prior chemotherapy regimens	
Reporting group title	Arm A2
Reporting group description: Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have not received prior chemotherapy regimen	
Reporting group title	Arm B
Reporting group description: Nivolumab 360 mg IV Q3W + Docetaxel 75 mg/m ² IV Q3W + Prednisone 5 mg PO BID	
Reporting group title	Arm C
Reporting group description: Nivolumab 480 mg IV Q4W + Enzalutamide 160 mg PO QD	

Reporting group values	Arm A1	Arm A2	Arm B
Number of subjects	88	71	84
Age categorical Units:			

Age Continuous Units: years			
arithmetic mean	66.6	70.7	70.3
standard deviation	± 8.3	± 9.7	± 7.6
Sex: Female, Male Units: Participants			
Female	0	0	0
Male	88	71	84
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	1	8
White	72	64	70
More than one race	0	0	0
Unknown or Not Reported	10	5	5

Reporting group values	Arm C	Total	
Number of subjects	49	292	
Age categorical Units:			

Age Continuous Units: years arithmetic mean standard deviation	69.8 ± 8.0	-	
Sex: Female, Male Units: Participants			
Female	0	0	
Male	49	292	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	2	15	
White	42	248	
More than one race	0	0	
Unknown or Not Reported	5	25	

End points

End points reporting groups

Reporting group title	Arm A1
Reporting group description: Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have at least 1 but no more than 2 prior chemotherapy regimens	
Reporting group title	Arm A2
Reporting group description: Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have not received prior chemotherapy regimen	
Reporting group title	Arm B
Reporting group description: Nivolumab 360 mg IV Q3W + Docetaxel 75 mg/m ² IV Q3W + Prednisone 5 mg PO BID	
Reporting group title	Arm C
Reporting group description: Nivolumab 480 mg IV Q4W + Enzalutamide 160 mg PO QD	

Primary: Objective Response Rate per Prostate Cancer Clinical Trials Working Group 3 (ORR-PCWG3)

End point title	Objective Response Rate per Prostate Cancer Clinical Trials Working Group 3 (ORR-PCWG3) ^[1]
End point description: Objective response rate per prostate cancer clinical trials working group 3 (ORR-PCWG3) for target lesions and assessed by MRI is the percentage of participants who have a confirmed complete or partial best overall response (BOR) per PCWG3 among treated participants who have measurable disease. HRD+ N=Number of subjects analyzed in HRD+ subgroup	
End point type	Primary
End point timeframe: Up to approximately 36 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: Only summary statistics planned for this endpoint

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58 ^[2]	39 ^[3]	45 ^[4]	18 ^[5]
Units: Percentage of participants				
number (confidence interval 95%)				
Overall	10.3 (3.9 to 21.2)	15.4 (5.9 to 30.5)	40.0 (25.7 to 55.7)	11.1 (1.4 to 34.7)
Homologous Recombination Deficiency (HRD+)	17.2 (5.8 to 35.8)	25.0 (8.7 to 49.1)	36.8 (16.3 to 61.6)	20.0 (0.5 to 71.6)

Notes:

[2] - HRD+ N= 29

[3] - HRD+ N= 20

[4] - HRD+ N= 19

[5] - HRD+ N= 5

Statistical analyses

No statistical analyses for this end point

Primary: Prostate-Specific Antigen Response Rate (RR-PSA)

End point title	Prostate-Specific Antigen Response Rate (RR-PSA) ^[6]
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End point description:

Prostate-specific antigen response rate (RR-PSA) is the percentage of treated participants with a 50% or greater decrease in PSA from baseline to the lowest post-baseline PSA result.

HRD+ N=Number of subjects analyzed in HRD+ subgroup

End point type	Primary
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End point timeframe:

Up to approximately 36 months

Notes:

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

Justification: Only summary statistics planned for this endpoint

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84 ^[7]	66 ^[8]	81 ^[9]	44 ^[10]
Units: Percentage of participants				
number (confidence interval 95%)				
Overall	11.9 (5.9 to 20.8)	27.3 (17.0 to 39.6)	46.9 (35.7 to 58.3)	34.1 (20.5 to 49.9)
Homologous Recombination Deficiency (HRD+)	18.2 (8.2 to 32.7)	41.9 (24.5 to 60.9)	50.0 (32.4 to 67.6)	50.0 (18.7 to 81.3)

Notes:

[7] - HRD+ N= 44

[8] - HRD+ N= 31

[9] - HRD+ N= 34

[10] - HRD+ N= 10

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic Progression-Free Survival (rPFS)

End point title	Radiographic Progression-Free Survival (rPFS)
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End point description:

Radiographic progress-free survival (rPFS) is the time between treatment initiation and the first date of documented progression or death due to any cause, whichever occurs

first assessed by the investigator per Prostate Cancer Clinical Trials Working Group 3 (PCWG3)

99999=NA

HRD+ N=Number of subjects analyzed in HRD+ subgroup

End point type	Secondary
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End point timeframe:

Up to approximately 84 months

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88 ^[11]	71 ^[12]	84 ^[13]	49 ^[14]
Units: Months				
median (confidence interval 95%)				
Overall	4.60 (3.68 to 5.72)	8.15 (5.59 to 10.97)	9.20 (8.25 to 11.47)	5.75 (3.81 to 9.33)
Homologous Recombination Deficiency (HRD+)	5.59 (3.68 to 8.08)	11.01 (6.74 to 12.02)	10.45 (8.44 to 12.88)	8.48 (3.78 to 99999)

Notes:

[11] - HRD+ N= 45

[12] - HRD+ N= 34

[13] - HRD+ N= 35

[14] - HRD+ N= 12

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response per Prostate Cancer Clinical Trials Working Group 3 (TTR-PCWG3)

End point title	Time to Response per Prostate Cancer Clinical Trials Working Group 3 (TTR-PCWG3)
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End point description:

Time to response per prostate cancer clinical trials working group 3 (TTR-PCWG3) is the time from treatment initiation to the date of the first documented complete response (CR) or partial response (PR) per Prostate Cancer Clinical Trials Working Group 3 (PCWG3).

HRD+ N=Number of subjects analyzed in HRD+ subgroup

End point type	Secondary
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End point timeframe:

Up to approximately 84 months

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 ^[15]	6 ^[16]	21 ^[17]	2 ^[18]
Units: Months				
median (full range (min-max))				
Overall	1.94 (1.6 to 5.1)	1.95 (1.8 to 11.0)	1.94 (1.6 to 8.3)	1.9 (1.9 to 1.9)
Homologous Recombination Deficiency (HRD+)	2.76 (1.6 to 5.1)	2.07 (1.8 to 11.0)	2.04 (1.8 to 8.3)	1.9 (1.9 to 1.9)

Notes:

[15] - HRD+ N+ 6

[16] - HRD+ N= 5

[17] - HRD+ N= 9

[18] - HRD+ N= 1

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response per Prostate Cancer Clinical Trials Working Group 3 (DOR-PCWG3)

End point title	Duration of Response per Prostate Cancer Clinical Trials Working Group 3 (DOR-PCWG3)
End point description: Duration of response per prostate cancer clinical trials working group 3 (DOR-PCWG3) is the time between the date of first response (complete response/partial response per PCWG3) to the date of first documented radiographic progression per Prostate Cancer Clinical Trials Working Group 3 (PCWG3) or death due to any cause. 99999=NA HRD+ N=Number of subjects analyzed in HRD+ subgroup	
End point type	Secondary
End point timeframe: Up to approximately 84 months	

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7 ^[19]	6 ^[20]	21 ^[21]	2 ^[22]
Units: Months				
median (confidence interval 95%)				
Overall	99999 (3.45 to 99999)	7.10 (3.78 to 99999)	7.21 (6.47 to 12.35)	99999 (9.23 to 99999)
Homologous Recombination Deficiency (HRD+)	99999 (3.45 to 99999)	7.10 (3.78 to 99999)	7.43 (6.44 to 13.86)	99999 (99999 to 99999)

Notes:

[19] - HRD+ N= 6

[20] - HRD+ N= 5

[21] - HRD+ N= 9

[22] - HRD+ N= 1

Statistical analyses

No statistical analyses for this end point

Secondary: Prostate-Specific Antigen Time to Progression (TTP-PSA)

End point title	Prostate-Specific Antigen Time to Progression (TTP-PSA)
End point description: Prostate-specific antigen time to progression (TTP-PSA) is the time between treatment initiation to the date of PSA progression per prostate cancer clinical trials working group 3 (PCWG3). HRD+ N=Number of subjects analyzed in HRD+ subgroup	
End point type	Secondary
End point timeframe: Up to approximately 84 months	

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85 ^[23]	66 ^[24]	81 ^[25]	44 ^[26]
Units: Months				
median (confidence interval 95%)				
Overall	3.78 (2.83 to 6.47)	3.45 (2.83 to 6.21)	8.67 (7.16 to 10.35)	3.09 (2.79 to 6.37)
Homologous Recombination Deficiency (HRD+)	6.47 (3.78 to 9.63)	10.25 (4.63 to 13.77)	8.64 (7.16 to 10.58)	5.55 (2.73 to 8.28)

Notes:

[23] - HRD+ N= 44

[24] - HRD+ N= 32

[25] - HRD+ N= 34

[26] - HRD+ N= 10

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Overall Survival (OS) is the time between treatment initiation and the date of death from any cause. For participants who are alive, their survival time will be censored at the last date that they were known to be alive. OS will be censored for participants at the date of treatment initiation if they had no follow-up. HRD+ N=Number of subjects analyzed in HRD+ subgroup	
End point type	Secondary
End point timeframe:	
Up to approximately 84 months	

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88 ^[27]	71 ^[28]	84 ^[29]	49 ^[30]
Units: Months				
median (confidence interval 95%)				
Overall	13.96 (10.35 to 15.77)	20.24 (13.54 to 22.90)	18.17 (15.15 to 25.49)	17.41 (12.98 to 24.15)
Homologous Recombination Deficiency (HRD+)	15.15 (11.40 to 18.20)	23.00 (13.54 to 29.27)	19.35 (13.54 to 27.20)	24.97 (9.10 to 45.50)

Notes:

[27] - HRD+ N= 45

[28] - HRD+ N= 34

[29] - HRD+ N= 35

[30] - HRD+ N= 12

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)
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End point description:

Number of Participants with any grade adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation, and immune-mediated AEs using the Common Toxicity Criteria Grade for Adverse Events (CTCAE V4)

End point type	Secondary
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End point timeframe:

From first dose to up to 30 days post last dose (Up to 82 months)

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	71	84	49
Units: Participants				
Adverse Events (AEs)	88	71	83	49
Serious Adverse Events (SAEs)	49	37	41	20
AEs leading to discontinuation	47	31	37	17
Immune-mediated AEs (Pneumonitis)	1	2	9	0
Immune-mediated AEs (Diarrhea/Colitis)	3	4	2	0
Immune-mediated AEs (Hepatitis)	8	6	1	2
Immune-mediated AEs (Nephritis/Renal Dysfunction)	0	3	0	0
Immune-mediated AEs (Rash)	6	5	7	10
Immune-mediated AEs (Hypersensitivity)	0	0	0	3
Immune-mediated AEs (Adrenal insufficiency)	1	0	0	0
Immune-mediated AEs (Hypothyroidism/Thyroiditis)	7	6	3	5
Immune-mediated AEs (Hyperthyroidism)	2	1	2	0
Immune-mediated AEs (Hypophysitis)	0	0	1	0
Immune-mediated AEs (Diabetes Mellitus)	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Died

End point title	Number of Participants who Died
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End point description:

Number of participants who died due to any cause.

End point type	Secondary
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End point timeframe:

Up to 84 months

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	71	84	49
Units: Participants	79	66	76	47

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Abnormalities in Specific Liver Tests

End point title	Number of Participants with Laboratory Abnormalities in Specific Liver Tests
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End point description:

Number of participants with laboratory abnormalities in specific liver tests based on SI conventional units to assess the overall safety and tolerability of BMS-986213 in combination with chemotherapy vs. Nivolumab in combination with chemotherapy. The number of participants with the following laboratory abnormalities from on-treatment evaluations will be summarized:

- ALT or AST > 3 x ULN, > 5 x ULN, > 10 x ULN and > 20 x ULN
- Total bilirubin > 2 x ULN
- ALP > 1.5 x ULN
- Concurrent (within 1 day) ALT or AST > 3 x ULN and total bilirubin > 1.5 x ULN
- Concurrent (within 30 days) ALT or AST > 3 x ULN and total bilirubin > 1.5 x ULN
- Concurrent (within 1 day) ALT or AST > 3 x ULN and total bilirubin > 2 x ULN
- Concurrent (within 30 days) ALT or AST > 3 x ULN and total bilirubin > 2 x ULN

End point type	Secondary
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End point timeframe:

From first dose to up to 30 days post last dose (up to 82 months)

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	69	84	48
Units: Participants				
ALT or AST > 3xULN	19	23	6	4
ALT or AST > 5xULN	11	15	3	3
ALT or AST > 10xULN	2	5	1	0
ALT or AST > 20xULN	0	1	1	0
TOTAL BILIRUBIN > 2xULN	3	1	1	0
ALP > 1.5xULN	49	34	35	22
ALT/AST>3xULN Bilirubin>1.5xULN within 1 day	3	1	0	1
ALT/AST> 3xULN Bilirubin>1.5xULN within 30 days	4	1	0	1
ALT/AST>3xULN Bilirubin>2xULN within 1 day	2	1	0	0
ALT/AST>3xULN Bilirubin>2xULN within 30 days	2	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Abnormalities in Specific Thyroid Tests

End point title	Number of Participants with Laboratory Abnormalities in Specific Thyroid Tests
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End point description:

Number of participants with laboratory abnormalities in specific thyroid tests based on US conventional units. The number of participants with the following laboratory abnormalities from on-treatment evaluations will be summarized:

- TSH value > ULN and
 - with baseline TSH value <= ULN
 - with at least one FT3/FT4 test value < LLN within 2-week window after the abnormal TSH test
 - with all FT3/FT4 test values >= LLN within 2-week window after the abnormal TSH test
 - with FT3/FT4 missing within 2-week window after the abnormal TSH test.
- TSH < LLN and
 - with baseline TSH value >= LLN
 - with at least one FT3/FT4 test value > ULN within 2-week window after the abnormal TSH test
 - with all FT3/FT4 test values <= ULN within 2-week window after the abnormal TSH test
 - with FT3/FT4 missing within 2-week window after the abnormal TSH test

End point type	Secondary
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End point timeframe:

From first dose to up to 30 days post last dose (Up to 82 months)

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	71	84	49
Units: Participants				
TSH > ULN	23	17	12	17
TSH > ULN with TSH <= ULN at baseline	18	12	7	12
TSH>ULN with at least one FT3/FT4 test value<LLN	10	6	7	5
TSH>ULN with all other FT3/FT4 test values>= LLN	11	9	3	9
TSH>ULN with FT3/FT4 test missing	2	2	2	3
TSH < LLN	17	12	25	8
TSH < LLN with TSH >= LLN at baseline	14	11	19	8
TSH<LLN with at least one FT3/FT4 test value>ULN	6	5	2	7
TSH<LLN with all other FT3/FT4 test values<= ULN	8	4	11	0
TSH < LLN with FT3/FT4 test missing	3	3	12	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Laboratory Values Change from Baseline

End point title	Number of Participants with Laboratory Values Change from
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End point description:

Number of participants changed from baseline in laboratory values of worst toxicity grade (grade 0= wnl, grade 1= mild, grade 2= moderate, grade 3= severe) based on US conventional units by cohort. 99999=NA

End point type

Secondary

End point timeframe:

From first dose to up to 30 days post last dose (Up to 82 months)

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	71	84	49
Units: Participants				
Hemoglobin Grade 0	23	21	30	8
Hemoglobin Grade 1	38	28	23	13
Hemoglobin Grade 2	8	3	2	2
Platelet Grade 0	34	32	10	13
Platelet Grade 1	4	1	0	0
Leukocytes Grade 0	39	35	30	13
Leukocytes Grade 1	10	6	3	3
Leukocytes Grade 2	1	0	1	99999
Lymphocytes Grade 0	24	30	28	14
Lymphocytes Grade 1	11	8	1	2
Lymphocytes Grade 2	3	3	6	3
Lymphocytes Grade 3	1	0	0	99999
Neutrophil Grade 0	35	26	38	7
Neutrophil Grade 1	3	4	1	99999
Neutrophil Grade 2	1	99999	99999	1
Alkaline Phosphatase Grade 0	25	34	13	8
Alkaline Phosphatase Grade 1	14	4	13	6
Alkaline Phosphatase Grade 2	9	1	3	0
Alkaline Phosphatase Grade 3	1	3	0	0
Aspartate Aminotransferase Grade 0	52	49	16	9
Aspartate Aminotransferase Grade 1	5	4	6	4
Alanine Aminotransferase Grade 0	48	48	13	4
Alanine Aminotransferase Grade 1	4	3	3	1
Bilirubin Grade 0	16	12	2	3
Bilirubin Grade 1	1	99999	99999	0
Creatinine Grade 0	31	30	13	3
Creatinine Grade 1	7	5	5	2

Statistical analyses

No statistical analyses for this end point

Post-hoc: Objective Response Rate per Prostate Cancer Clinical Trials Working Group 3 (ORR-PCWG3) - Extended Collection

End point title	Objective Response Rate per Prostate Cancer Clinical Trials Working Group 3 (ORR-PCWG3) - Extended Collection
End point description: Objective response rate per prostate cancer clinical trials working group 3 (ORR-PCWG3) for target lesions and assessed by MRI is the percentage of participants who have a confirmed complete or partial best overall response (BOR) per PCWG3 among treated participants who have measurable disease. HRD+ N=Number of subjects analyzed in HRD+ subgroup	
End point type	Post-hoc
End point timeframe: Up to approximately 82 months	

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58 ^[31]	39 ^[32]	45 ^[33]	18 ^[34]
Units: Percentage of participants				
number (confidence interval 95%)				
Overall	12.1 (5.0 to 23.3)	15.4 (5.9 to 30.5)	40.0 (25.7 to 55.7)	11.1 (1.4 to 34.7)
Homologous Recombination Deficiency (HRD+)	20.7 (8.0 to 39.7)	25.0 (8.7 to 49.1)	36.8 (16.3 to 61.6)	20.0 (0.5 to 71.6)

Notes:

[31] - HRD+ N= 29

[32] - HRD+ N= 20

[33] - HRD+ N= 19

[34] - HRD+ N= 5

Statistical analyses

No statistical analyses for this end point

Post-hoc: Prostate-Specific Antigen Response Rate (RR-PSA) - Extended Collection

End point title	Prostate-Specific Antigen Response Rate (RR-PSA) - Extended Collection
End point description: Prostate-specific antigen response rate (RR-PSA) is the percentage of treated participants with a 50% or greater decrease in PSA from baseline to the lowest post-baseline PSA result. HRD+ N=Number of subjects analyzed in HRD+ subgroup	
End point type	Post-hoc
End point timeframe: Up to approximately 82 months	

End point values	Arm A1	Arm A2	Arm B	Arm C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85 ^[35]	66 ^[36]	81 ^[37]	44 ^[38]
Units: Percentage of participants				
number (confidence interval 95%)				
Overall	11.8 (5.8 to 20.6)	28.8 (18.3 to 41.3)	46.9 (35.7 to 58.3)	34.1 (20.5 to 49.9)

Homologous Recombination Deficiency (HRD+)	18.2 (8.2 to 32.7)	43.8 (26.4 to 62.3)	50.0 (32.4 to 67.6)	50.0 (18.7 to 81.3)
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Notes:

[35] - HRD+ N= 44

[36] - HRD+ N= 32

[37] - HRD+ N= 34

[38] - HRD+ N= 10

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for all-cause mortality from their first dose to their study completion (up to approximately 84 months). SAEs and Other AEs were assessed from first dose to 100 days post the last dose (up to approximately 84 months).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Arm A1
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Reporting group description:

Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have at least 1 but no more than 2 prior chemotherapy regimens

Reporting group title	Arm C
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Reporting group description:

Nivolumab 480 mg IV Q4W + Enzalutamide 160 mg PO QD

Reporting group title	Arm B
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Reporting group description:

Nivolumab 360 mg IV Q3W + Docetaxel 75 mg/m² IV Q3W + Prednisone 5 mg PO BID

Reporting group title	Arm A2
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Reporting group description:

Nivolumab 480 mg IV Q4W + Rucaparib 600 mg PO BID for participants who have not received prior chemotherapy regimen

Serious adverse events	Arm A1	Arm C	Arm B
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 88 (60.23%)	25 / 49 (51.02%)	50 / 84 (59.52%)
number of deaths (all causes)	79	47	76
number of deaths resulting from adverse events	21	8	17
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Cancer pain			

subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon neoplasm			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head and neck cancer			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Malignant neoplasm progression			
subjects affected / exposed	14 / 88 (15.91%)	7 / 49 (14.29%)	8 / 84 (9.52%)
occurrences causally related to treatment / all	0 / 14	0 / 7	0 / 8
deaths causally related to treatment / all	0 / 14	0 / 6	0 / 7
Metastases to bone			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Prostate cancer			
subjects affected / exposed	1 / 88 (1.14%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Second primary malignancy			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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			
Peripheral artery thrombosis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Haematoma			

subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Lymphatic fistula			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Lymphoedema			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
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 / 88 (0.00%)	1 / 49 (2.04%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	2 / 88 (2.27%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Malaise			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
General physical health deterioration			
subjects affected / exposed	3 / 88 (3.41%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Hypersensitivity			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular mass			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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			
Aspiration			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Cough			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottic oedema			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Hypoxia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 88 (1.14%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	4 / 84 (4.76%)
occurrences causally related to treatment / all	1 / 1	0 / 0	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Productive cough			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Immune-mediated lung disease			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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			
Confusional state			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abnormal behaviour			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			

Device occlusion			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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	1 / 88 (1.14%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
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 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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 condition abnormal			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Liver function test abnormal			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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

Liver function test increased subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Neutrophil count decreased subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Injury, poisoning and procedural complications			
Ureteric anastomosis complication subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Limb injury subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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 / 88 (0.00%)	2 / 49 (4.08%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular anastomosis aneurysm subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fall			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure			

subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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			
Presyncope			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal ganglia infarction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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	1 / 88 (1.14%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Hyperaesthesia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Nervous system disorder			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Seizure			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Spinal cord compression			

subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	0 / 84 (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
Syncope			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Febrile neutropenia			
subjects affected / exposed	4 / 88 (4.55%)	0 / 49 (0.00%)	4 / 84 (4.76%)
occurrences causally related to treatment / all	3 / 4	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Anaemia			
subjects affected / exposed	8 / 88 (9.09%)	2 / 49 (4.08%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	6 / 8	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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	4 / 88 (4.55%)	0 / 49 (0.00%)	4 / 84 (4.76%)
occurrences causally related to treatment / all	4 / 4	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Vertigo			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Colitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
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 ulcerative			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	3 / 88 (3.41%)	0 / 49 (0.00%)	3 / 84 (3.57%)
occurrences causally related to treatment / all	3 / 3	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Faecaloma			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Haematochezia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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	3 / 88 (3.41%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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	2 / 88 (2.27%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Ileus paralytic			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	0 / 84 (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
Hepatic cytolysis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			

subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Hepatotoxicity			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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			
Cutaneous sarcoidosis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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			
subjects affected / exposed	0 / 88 (0.00%)	2 / 49 (4.08%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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 morbilliform			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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			
Bladder obstruction			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Acute kidney injury			

subjects affected / exposed	7 / 88 (7.95%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	4 / 7	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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	2 / 88 (2.27%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Immune-mediated nephritis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric compression			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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 obstruction			

subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Urinoma			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	3 / 88 (3.41%)	2 / 49 (4.08%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
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 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Periarthritis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	0 / 84 (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
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Atypical pneumonia			

subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary sepsis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Cellulitis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Cellulitis orbital			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Catheter site cellulitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Septic shock			

subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Sepsis			
subjects affected / exposed	2 / 88 (2.27%)	1 / 49 (2.04%)	3 / 84 (3.57%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 88 (2.27%)	2 / 49 (4.08%)	6 / 84 (7.14%)
occurrences causally related to treatment / all	0 / 4	0 / 2	4 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 3
Neutropenic infection			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Influenza			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Urosepsis			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 88 (2.27%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
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	3 / 88 (3.41%)	0 / 49 (0.00%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			

subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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
Hypercalcaemia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Hyperglycaemia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	0 / 84 (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	0 / 88 (0.00%)	1 / 49 (2.04%)	0 / 84 (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
Hypophosphataemia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm A2		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	45 / 71 (63.38%)		
number of deaths (all causes)	66		
number of deaths resulting from adverse events	17		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colon neoplasm			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head and neck cancer			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 9		
Metastases to bone			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			

subjects affected / exposed	3 / 71 (4.23%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Second primary malignancy			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphatic fistula			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphoedema			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Asthenia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Immune system disorders				

Sarcoidosis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Testicular mass			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epiglottic oedema			

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 71 (2.82%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pleural effusion				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Productive cough				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated lung disease				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				

subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hallucination			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abnormal behaviour			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device occlusion			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood creatinine increased subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram T wave inversion subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical condition abnormal subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver function test increased subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ureteric anastomosis complication subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pelvic fracture			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular anastomosis aneurysm			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic valve stenosis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal ganglia infarction			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperaesthesia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorder			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Trigeminal neuralgia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Febrile neutropenia			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain upper				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Faecaloma				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obstructive pancreatitis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated enterocolitis			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cytolysis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Autoimmune hepatitis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Cutaneous sarcoidosis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash morbilliform			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Bladder obstruction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Autoimmune nephritis			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated nephritis			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Proteinuria			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureteric compression			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinoma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureteric obstruction			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Back pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar spinal stenosis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	3 / 71 (4.23%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myositis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periarthritis				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Spinal pain				

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biliary sepsis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis orbital			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Catheter site cellulitis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Rectal abscess			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia			

subjects affected / exposed	9 / 71 (12.68%)			
occurrences causally related to treatment / all	1 / 11			
deaths causally related to treatment / all	0 / 2			
Neutropenic infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	2 / 71 (2.82%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	3 / 71 (4.23%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A1	Arm C	Arm B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 88 (98.86%)	48 / 49 (97.96%)	83 / 84 (98.81%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 88 (5.68%)	4 / 49 (8.16%)	5 / 84 (5.95%)
occurrences (all)	6	4	6
Hypotension			
subjects affected / exposed	7 / 88 (7.95%)	1 / 49 (2.04%)	4 / 84 (4.76%)
occurrences (all)	8	1	8
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	24 / 88 (27.27%)	11 / 49 (22.45%)	17 / 84 (20.24%)
occurrences (all)	32	13	26
Chills			

subjects affected / exposed	4 / 88 (4.55%)	1 / 49 (2.04%)	9 / 84 (10.71%)
occurrences (all)	4	1	10
Fatigue			
subjects affected / exposed	36 / 88 (40.91%)	21 / 49 (42.86%)	41 / 84 (48.81%)
occurrences (all)	44	27	55
Mucosal inflammation			
subjects affected / exposed	8 / 88 (9.09%)	1 / 49 (2.04%)	6 / 84 (7.14%)
occurrences (all)	9	1	12
Oedema peripheral			
subjects affected / exposed	17 / 88 (19.32%)	10 / 49 (20.41%)	20 / 84 (23.81%)
occurrences (all)	19	12	25
Pain			
subjects affected / exposed	6 / 88 (6.82%)	7 / 49 (14.29%)	3 / 84 (3.57%)
occurrences (all)	7	7	5
Pyrexia			
subjects affected / exposed	15 / 88 (17.05%)	4 / 49 (8.16%)	13 / 84 (15.48%)
occurrences (all)	16	4	14
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	8 / 84 (9.52%)
occurrences (all)	0	0	8
Epistaxis			
subjects affected / exposed	1 / 88 (1.14%)	2 / 49 (4.08%)	6 / 84 (7.14%)
occurrences (all)	1	2	6
Dyspnoea exertional			
subjects affected / exposed	4 / 88 (4.55%)	1 / 49 (2.04%)	5 / 84 (5.95%)
occurrences (all)	4	1	5
Dyspnoea			
subjects affected / exposed	13 / 88 (14.77%)	4 / 49 (8.16%)	20 / 84 (23.81%)
occurrences (all)	15	4	24
Cough			
subjects affected / exposed	15 / 88 (17.05%)	2 / 49 (4.08%)	21 / 84 (25.00%)
occurrences (all)	15	2	25
Psychiatric disorders			

Depression subjects affected / exposed occurrences (all)	2 / 88 (2.27%) 2	4 / 49 (8.16%) 4	2 / 84 (2.38%) 2
Insomnia subjects affected / exposed occurrences (all)	8 / 88 (9.09%) 8	8 / 49 (16.33%) 9	9 / 84 (10.71%) 10
Investigations			
Weight decreased subjects affected / exposed occurrences (all)	9 / 88 (10.23%) 9	5 / 49 (10.20%) 6	6 / 84 (7.14%) 6
Transaminases increased subjects affected / exposed occurrences (all)	3 / 88 (3.41%) 3	1 / 49 (2.04%) 1	2 / 84 (2.38%) 2
Platelet count decreased subjects affected / exposed occurrences (all)	4 / 88 (4.55%) 4	1 / 49 (2.04%) 1	0 / 84 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	0 / 49 (0.00%) 0	6 / 84 (7.14%) 7
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	15 / 88 (17.05%) 22	7 / 49 (14.29%) 8	4 / 84 (4.76%) 6
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	8 / 88 (9.09%) 9	5 / 49 (10.20%) 6	4 / 84 (4.76%) 4
Blood creatinine increased subjects affected / exposed occurrences (all)	8 / 88 (9.09%) 10	2 / 49 (4.08%) 4	5 / 84 (5.95%) 5
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	16 / 88 (18.18%) 22	4 / 49 (8.16%) 5	5 / 84 (5.95%) 6
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	2 / 88 (2.27%) 2	2 / 49 (4.08%) 2	6 / 84 (7.14%) 10
Nervous system disorders			

Dizziness			
subjects affected / exposed	7 / 88 (7.95%)	6 / 49 (12.24%)	17 / 84 (20.24%)
occurrences (all)	7	7	19
Dysgeusia			
subjects affected / exposed	11 / 88 (12.50%)	6 / 49 (12.24%)	12 / 84 (14.29%)
occurrences (all)	12	6	14
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	5 / 84 (5.95%)
occurrences (all)	1	0	5
Paraesthesia			
subjects affected / exposed	2 / 88 (2.27%)	3 / 49 (6.12%)	3 / 84 (3.57%)
occurrences (all)	2	3	3
Neuropathy peripheral			
subjects affected / exposed	2 / 88 (2.27%)	2 / 49 (4.08%)	23 / 84 (27.38%)
occurrences (all)	2	2	24
Headache			
subjects affected / exposed	8 / 88 (9.09%)	6 / 49 (12.24%)	10 / 84 (11.90%)
occurrences (all)	9	6	13
Syncope			
subjects affected / exposed	0 / 88 (0.00%)	3 / 49 (6.12%)	3 / 84 (3.57%)
occurrences (all)	0	3	3
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	5 / 88 (5.68%)	1 / 49 (2.04%)	2 / 84 (2.38%)
occurrences (all)	12	1	3
Anaemia			
subjects affected / exposed	32 / 88 (36.36%)	15 / 49 (30.61%)	25 / 84 (29.76%)
occurrences (all)	57	22	32
Thrombocytopenia			
subjects affected / exposed	11 / 88 (12.50%)	3 / 49 (6.12%)	2 / 84 (2.38%)
occurrences (all)	18	3	2
Neutropenia			
subjects affected / exposed	14 / 88 (15.91%)	0 / 49 (0.00%)	14 / 84 (16.67%)
occurrences (all)	28	0	14
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	29 / 88 (32.95%)	9 / 49 (18.37%)	42 / 84 (50.00%)
occurrences (all)	43	11	65
Dyspepsia			
subjects affected / exposed	3 / 88 (3.41%)	3 / 49 (6.12%)	4 / 84 (4.76%)
occurrences (all)	3	3	5
Nausea			
subjects affected / exposed	46 / 88 (52.27%)	17 / 49 (34.69%)	36 / 84 (42.86%)
occurrences (all)	65	18	51
Vomiting			
subjects affected / exposed	30 / 88 (34.09%)	5 / 49 (10.20%)	14 / 84 (16.67%)
occurrences (all)	45	5	20
Abdominal pain upper			
subjects affected / exposed	4 / 88 (4.55%)	1 / 49 (2.04%)	4 / 84 (4.76%)
occurrences (all)	4	1	4
Abdominal pain			
subjects affected / exposed	9 / 88 (10.23%)	3 / 49 (6.12%)	11 / 84 (13.10%)
occurrences (all)	9	3	12
Constipation			
subjects affected / exposed	26 / 88 (29.55%)	10 / 49 (20.41%)	21 / 84 (25.00%)
occurrences (all)	34	12	25
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	10 / 88 (11.36%)	6 / 49 (12.24%)	16 / 84 (19.05%)
occurrences (all)	11	10	19
Rash maculo-papular			
subjects affected / exposed	1 / 88 (1.14%)	4 / 49 (8.16%)	4 / 84 (4.76%)
occurrences (all)	1	6	4
Skin lesion			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	1 / 84 (1.19%)
occurrences (all)	2	0	1
Nail discolouration			
subjects affected / exposed	0 / 88 (0.00%)	0 / 49 (0.00%)	7 / 84 (8.33%)
occurrences (all)	0	0	7
Erythema			

subjects affected / exposed occurrences (all)	4 / 88 (4.55%) 4	1 / 49 (2.04%) 1	1 / 84 (1.19%) 1
Dry skin subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 6	4 / 49 (8.16%) 4	3 / 84 (3.57%) 3
Alopecia subjects affected / exposed occurrences (all)	0 / 88 (0.00%) 0	1 / 49 (2.04%) 1	28 / 84 (33.33%) 28
Pruritus subjects affected / exposed occurrences (all)	10 / 88 (11.36%) 11	9 / 49 (18.37%) 9	6 / 84 (7.14%) 6
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	3 / 88 (3.41%) 3	1 / 49 (2.04%) 1	5 / 84 (5.95%) 5
Haematuria subjects affected / exposed occurrences (all)	7 / 88 (7.95%) 7	1 / 49 (2.04%) 1	5 / 84 (5.95%) 6
Acute kidney injury subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5	1 / 49 (2.04%) 1	0 / 84 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	7 / 88 (7.95%) 8	5 / 49 (10.20%) 5	4 / 84 (4.76%) 4
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	4 / 88 (4.55%) 4	0 / 49 (0.00%) 0	5 / 84 (5.95%) 5
Bone pain subjects affected / exposed occurrences (all)	12 / 88 (13.64%) 13	11 / 49 (22.45%) 13	8 / 84 (9.52%) 8
Back pain subjects affected / exposed occurrences (all)	20 / 88 (22.73%) 20	12 / 49 (24.49%) 12	25 / 84 (29.76%) 27
Arthralgia			

subjects affected / exposed	17 / 88 (19.32%)	16 / 49 (32.65%)	20 / 84 (23.81%)
occurrences (all)	18	19	25
Muscular weakness			
subjects affected / exposed	1 / 88 (1.14%)	2 / 49 (4.08%)	4 / 84 (4.76%)
occurrences (all)	1	2	4
Spinal pain			
subjects affected / exposed	0 / 88 (0.00%)	4 / 49 (8.16%)	2 / 84 (2.38%)
occurrences (all)	0	4	2
Pain in extremity			
subjects affected / exposed	7 / 88 (7.95%)	11 / 49 (22.45%)	10 / 84 (11.90%)
occurrences (all)	7	11	10
Myalgia			
subjects affected / exposed	4 / 88 (4.55%)	5 / 49 (10.20%)	4 / 84 (4.76%)
occurrences (all)	5	5	6
Musculoskeletal pain			
subjects affected / exposed	6 / 88 (6.82%)	1 / 49 (2.04%)	1 / 84 (1.19%)
occurrences (all)	6	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 88 (5.68%)	0 / 49 (0.00%)	5 / 84 (5.95%)
occurrences (all)	5	0	5
Pneumonia			
subjects affected / exposed	6 / 88 (6.82%)	1 / 49 (2.04%)	2 / 84 (2.38%)
occurrences (all)	7	1	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 88 (1.14%)	0 / 49 (0.00%)	5 / 84 (5.95%)
occurrences (all)	1	0	7
Urinary tract infection			
subjects affected / exposed	5 / 88 (5.68%)	3 / 49 (6.12%)	6 / 84 (7.14%)
occurrences (all)	5	3	8
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	29 / 88 (32.95%)	14 / 49 (28.57%)	25 / 84 (29.76%)
occurrences (all)	34	18	29
Hypophosphataemia			

subjects affected / exposed	3 / 88 (3.41%)	3 / 49 (6.12%)	1 / 84 (1.19%)
occurrences (all)	3	3	1
Hypomagnesaemia			
subjects affected / exposed	3 / 88 (3.41%)	3 / 49 (6.12%)	2 / 84 (2.38%)
occurrences (all)	3	4	2
Hypokalaemia			
subjects affected / exposed	4 / 88 (4.55%)	1 / 49 (2.04%)	4 / 84 (4.76%)
occurrences (all)	8	1	7
Hyperglycaemia			
subjects affected / exposed	2 / 88 (2.27%)	6 / 49 (12.24%)	6 / 84 (7.14%)
occurrences (all)	5	14	11
Dehydration			
subjects affected / exposed	2 / 88 (2.27%)	0 / 49 (0.00%)	4 / 84 (4.76%)
occurrences (all)	2	0	4

Non-serious adverse events	Arm A2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 71 (98.59%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Hypotension			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	7		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 71 (16.90%)		
occurrences (all)	13		
Chills			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	6		
Fatigue			
subjects affected / exposed	26 / 71 (36.62%)		
occurrences (all)	35		
Mucosal inflammation			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	15 / 71 (21.13%)		
occurrences (all)	17		
Pain			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	7 / 71 (9.86%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	9		
Cough			
subjects affected / exposed	11 / 71 (15.49%)		
occurrences (all)	12		
Psychiatric disorders			
Depression			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	6		
Insomnia			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	8		
Investigations			

Weight decreased subjects affected / exposed occurrences (all)	7 / 71 (9.86%) 7		
Transaminases increased subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 4		
Platelet count decreased subjects affected / exposed occurrences (all)	6 / 71 (8.45%) 9		
Neutrophil count decreased subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 4		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	21 / 71 (29.58%) 36		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	9 / 71 (12.68%) 10		
Blood creatinine increased subjects affected / exposed occurrences (all)	20 / 71 (28.17%) 24		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	21 / 71 (29.58%) 35		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 6		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	6 / 71 (8.45%) 9		
Dysgeusia subjects affected / exposed occurrences (all)	9 / 71 (12.68%) 9		
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Neuropathy peripheral			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	7		
Syncope			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Anaemia			
subjects affected / exposed	30 / 71 (42.25%)		
occurrences (all)	39		
Thrombocytopenia			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	9		
Neutropenia			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	7		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	21 / 71 (29.58%)		
occurrences (all)	42		
Dyspepsia			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Nausea			

subjects affected / exposed	35 / 71 (49.30%)		
occurrences (all)	45		
Vomiting			
subjects affected / exposed	18 / 71 (25.35%)		
occurrences (all)	30		
Abdominal pain upper			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	7		
Abdominal pain			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	18 / 71 (25.35%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	11		
Rash maculo-papular			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	4		
Skin lesion			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Nail discolouration			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Dry skin			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	5		
Alopecia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	4		

Pruritus subjects affected / exposed occurrences (all)	11 / 71 (15.49%) 14		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all) Haematuria subjects affected / exposed occurrences (all) Acute kidney injury subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 4 3 / 71 (4.23%) 4 0 / 71 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 5		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Spinal pain subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0 7 / 71 (9.86%) 7 11 / 71 (15.49%) 13 11 / 71 (15.49%) 13 6 / 71 (8.45%) 6 0 / 71 (0.00%) 0		

Pain in extremity subjects affected / exposed occurrences (all)	7 / 71 (9.86%) 8		
Myalgia subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 5		
Musculoskeletal pain subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 3		
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1		
Pneumonia subjects affected / exposed occurrences (all)	6 / 71 (8.45%) 7		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 4		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	21 / 71 (29.58%) 25		
Hypophosphataemia subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 7		
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 5		
Hyperglycaemia			

subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2018	Clarification to the inclusion and exclusion criteria
10 September 2018	Study design update
31 January 2019	Timing of final analysis clarification
08 August 2019	Interim Analysis clarification

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported