Clinical trial results:
An Open-Label, Randomized, Phase 3 Clinical Trial of REGN2810 Versus Investigator's Choice of Chemotherapy in Recurrent or Metastatic Cervical Carcinoma

Summary

EudraCT number	2017-000350-19
Trial protocol	ES PL GB BE GR IT
Global end of trial date	20 April 2023

Results information

Result version number	v1 (current)
This version publication date	05 May 2024
First version publication date	05 May 2024

Trial information

Trial identification

Sponsor protocol code	R2810-ONC-1676

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc, 001 844-734-6643, clinicaltrials@regeneron.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	20 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare overall survival (OS) for participants with recurrent or metastatic cervical cancer who have histology of squamous cell carcinoma (SCC) and who had any eligible histology, treated with either cemiplimab or investigator's choice (IC) chemotherapy.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 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	Australia: 30
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Brazil: 89
Country: Number of subjects enrolled	Canada: 42
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Japan: 56
Country: Number of subjects enrolled	Korea, Republic of: 76
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Russian Federation: 85
Country: Number of subjects enrolled	Spain: 66
Country: Number of subjects enrolled	Taiwan: 34
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	608
EEA total number of subjects	170

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	533
From 65 to 84 years	73
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

752 participants were screened, 144 participants failed screening, 608 randomized to receive cemiplimab or investigator choice of chemotherapy (control treatment determined before randomization by investigator from options per protocol). Randomization was stratified

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
Arm title	Cemiplimab

Arm description:

Participants received a fixed dose of 350 milligrams (mg) of cemiplimab intravenous (IV) infusion on Day 1 of every 3 weeks (Q3W) for up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.

Arm type	Experimental
Investigational medicinal product name	LIBTAYO
Investigational medicinal product code	REGN2810
Other name	cemiplimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fixed Dose of 350 mg at a frequency of Day 1, every three weeks

Arm title	Investigator Choice (IC) Chemotherapy

Arm description:

Participants received IC of chemotherapy (options listed by class): (1) Antifolate: pemetrexed 500 mg per meter square (mg/m^2) on Day 1; (2) Topoisomerase 1 inhibitor: topotecan 1 mg/m^2 daily for 5 days, starting on Day 1 or irinotecan 100 mg/m^2 weekly (Days 1, 8, 15 and 22), followed by 10 to 14 days rest, for a 42-day (6-week) cycle; (3) Nucleoside analogue: gemcitabine 1000 mg/m^2 on Days 1 and 8; (4) Vinca alkaloid: vinorelbine 30 mg/m^2 IV infusion based on body surface area for Q3W up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.

Arm type	Active comparator
Investigational medicinal product name	Antifolate: Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mg/m^2, , body surface area Day 1 every 3 weeks for up to 96 weeks

Investigational medicinal product name	Topoisomerase 1 inhibitor: toptecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 1 mg/m^2 body surface area daily for 5 days, starting on Day 1 for three weeks (up to 96 weeks)	
Investigational medicinal product name	Vinca alkaloid: Vinorelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 30 mg/m^2 for a frequency of Days 1 and 8 for every three weeks, for up to 96 weeks	
Investigational medicinal product name	Nucleoside analogue: gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Dose: 1000 mg/m2 body surface area at a frequency of Days 1 and 8 every 3 weeks for up to 96 weeks	
Investigational medicinal product name	Topoisomerase 1 inhibitor: irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg/m^2 weekly (Days 1, 8, 15, and 22) followed by 10 to 14 days rest, for a 42-day (6-week) cycle for up to 96 weeks	

Number of subjects in period 1	Cemiplimab	Investigator Choice (IC) Chemotherapy
Started	304	304
Full Analysis Set (FAS)	304	304
Safety Analysis Set (SAF)	300	290
Completed Treatment	38	0
Completed	35	0
Not completed	269	304
Adverse event, serious fatal	96	98
Participant Decision	35	43
Physician decision	1	3
Non-compliance with Study Drug	-	2
Adverse event, non-fatal	17	7
Sponsor Decision	1	-
Unspecified	-	2
Lost to follow-up	2	2
Withdrawal of Participant	8	26
Disease Progression	109	121

Baseline characteristics

Reporting groups	
Reporting group title	Cemiplimab
Reporting group description:	
Participants received a fixed dose of 350 milligrams (mg) of cemiplimab intravenous (IV) infusion on Day 1 of every 3 weeks (Q3W) for up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.	
Reporting group title	Investigator Choice (IC) Chemotherapy
Reporting group description:	
Participants received IC of chemotherapy (options listed by class): (1) Antifolate: pemetrexed 500 mg per meter square (mg/m^2) on Day 1; (2) Topoisomerase 1 inhibitor: topotecan 1 mg/m^2 daily for 5 days, starting on Day 1 or irinotecan 100 mg/m^2 weekly (Days 1, 8, 15 and 22), followed by 10 to 14 days rest, for a 42-day (6-week) cycle; (3) Nucleoside analogue: gemcitabine 1000 mg/m^2 on Days 1 and 8; (4) Vinca alkaloid: vinorelbine 30 mg/m^2 IV infusion based on body surface area for Q3W up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.	

Reporting group values	Cemiplimab	Investigator Choice (IC) Chemotherapy	Total
Number of subjects	304	304	608
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	269	264	533
From 65-84 years	30	29	59
85 years and over	5	11	16
Age Continuous Units: years			
arithmetic mean	51.1	51.2	
standard deviation	± 11.59	± 11.77	-
Sex: Female, Male Units: Participants			
Female	304	304	608
Male	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	47	44	91
Not Hispanic or Latino	251	250	501
Unknown or Not Reported	6	10	16
Race/Ethnicity, Customized Units: Subjects			
White	193	192	385
Black or African American	9	12	21
Asian	88	88	176

American Indian or Alaska Native	2	1	3
Other	8	4	12
Unknown	1	1	2
Not Reported	3	6	9

End points

End points reporting groups

Reporting group title	Cemiplimab
Reporting group description:	
Participants received a fixed dose of 350 milligrams (mg) of cemiplimab intravenous (IV) infusion on Day 1 of every 3 weeks (Q3W) for up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.	
Reporting group title	Investigator Choice (IC) Chemotherapy
Reporting group description:	
Participants received IC of chemotherapy (options listed by class): (1) Antifolate: pemetrexed 500 mg per meter square (mg/m^2) on Day 1; (2) Topoisomerase 1 inhibitor: topotecan 1 mg/m^2 daily for 5 days, starting on Day 1 or irinotecan 100 mg/m^2 weekly (Days 1, 8, 15 and 22), followed by 10 to 14 days rest, for a 42-day (6-week) cycle; (3) Nucleoside analogue: gemcitabine 1000 mg/m^2 on Days 1 and 8; (4) Vinca alkaloid: vinorelbine 30 mg/m^2 IV infusion based on body surface area for Q3W up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Overall survival was defined as the time from randomization to the date of death due to any cause. A participant who had not died was censored at the last known date of contact.	
End point type	Primary
End point timeframe:	
Time from randomization to the date of death due to any cause (assessed up to 40 months)	

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	304		
Units: Months				
median (confidence interval 95%)	11.7 (9.6 to 13.4)	8.5 (7.5 to 9.6)		

Statistical analyses

Statistical analysis title	Stratified Log-rank Test
Comparison groups	Cemiplimab v Investigator Choice (IC) Chemotherapy
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority
Method	Stratified Log-rank Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.665

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.555
upper limit	0.796

Primary: Overall Survival (OS) in the SCC population

End point title	Overall Survival (OS) in the SCC population

End point description:

Overall survival was defined as the time from randomization to the date of death due to any cause. A participant who had not died was censored at the last known date of contact

End point type	Primary

End point timeframe:

Time from randomization to the date of death due to any cause (assessed up to 40 months)

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	238		
Units: Months				
median (confidence interval 95%)	10.9 (8.9 to 12.9)	8.8 (7.6 to 9.8)		

Statistical analyses

Statistical analysis title	Stratified Log-rank Test
Comparison groups	Cemiplimab v Investigator Choice (IC) Chemotherapy
Number of subjects included in analysis	477
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00024
Method	Stratified Log-rank Test
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.855

Secondary: Objective Response Rate (ORR) Assessed by Investigator Using RECIST 1.1

End point title	Objective Response Rate (ORR) Assessed by Investigator Using

	RECIST 1.1

End point description:

ORR was defined as the number of participants who achieved complete response (CR) or partial response (PR) as per RECIST 1.1. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<) 10 millimeters (mm) (<1 centimeter [cm]). PR: At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters.

End point type	Secondary

End point timeframe:

From date of randomization up to 40 months

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	304		
Units: Participants	52	19		

Statistical analyses

Statistical analysis title	Stratified Cochran-Mantel-Haenszel test
Comparison groups	Cemiplimab v Investigator Choice (IC) Chemotherapy
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	
Method	Stratified Cochran-Mantel-Haenszel test
Parameter estimate	Odds ratio (OR)
Point estimate	3.136
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.798
upper limit	5.468

Secondary: Progression-free Survival (PFS) Assessed by Investigator Using Response Evaluation Criteria in Solid Tumors (RECIST 1.1)

End point title	Progression-free Survival (PFS) Assessed by Investigator Using Response Evaluation Criteria in Solid Tumors (RECIST 1.1)

End point description:

PFS was defined as the time from randomization to the date of the first documented tumor progression (radiographic) or death due to any cause. Participants who do not have a documented tumor progression or death were censored on the date of their last evaluable tumor assessment.

End point type	Secondary

End point timeframe:

Time from randomization to the date of the first documented tumor progression or death due to any cause (assessed up to 40 months)

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	304		
Units: Months				
median (confidence interval 95%)	2.8 (2.6 to 3.9)	2.9 (2.7 to 3.5)		

Statistical analyses

Statistical analysis title	Stratified Log-rank Test
Comparison groups	Cemiplimab v Investigator Choice (IC) Chemotherapy
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.00031
Method	Stratified Log-rank Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.741
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.623
upper limit	0.882

Secondary: Duration of response (DOR) Assessed per RECIST 1.1

End point title	Duration of response (DOR) Assessed per RECIST 1.1

End point description:

DOR was defined as the time from the date of first response (CR or PR) to the date of the first documented progressive disease (per RECIST 1.1) or death due to any cause. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm (<1 cm). PR: At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters. Participants who never progressed while being followed was censored at the last valid tumor measurement. DOR was determined by Kaplan-Meier estimate. Here 'n' = the number of evaluable subjects at the specific point in time. Here 'n' = the number of evaluable participants

End point type	Secondary

End point timeframe:

Time from the date of first response to the date of the first documented progressive disease or death due to any cause (up to 40 months)

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	19		
Units: Months				
median (confidence interval 95%)	18.7 (16.4 to 99999)	7.2 (5.1 to 9.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, and TEAEs Leading to Death

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, and TEAEs Leading to Death

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. A TEAE was defined as those that are not present at baseline or represent the exacerbation of a pre-existing condition during the on-treatment period. A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in any of the following outcomes: death, life- threatening, required initial or prolonged in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. Any TEAE included participants with both serious and non-serious TEAEs. Number of participants with TEAEs, serious TEAEs, and TEAEs leading to death were reported. Here 'n' = the number of evaluable participants

End point type	Secondary

End point timeframe:

From date of randomization up to 40 months

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	300	290		
Units: Participants				
Participants with any TEAE	269	266		
Participants with any Serious TEAE	96	78		
Participants with any TEAE leading to Death	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life (QoL): Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30

(EORTC QLQ-C30) of Global Health Status /Quality of Life (GHS/QoL) and Physical Functioning Scales

End point title	Quality of Life (QoL): Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) of Global Health Status /Quality of Life (GHS/QoL) and Physical Functioning Scales

End point description:

EORTC QLQ-C30 is a 30-question tool used to assess the overall QoL in cancer participants. It consisted of 15 domains: 1 GHS/QoL scale, 5 functional scales (Physical, role, cognitive, emotional, social), and 9 symptom scales/items (Fatigue, nausea and vomiting, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, financial impact). Most items are scored 1 ("not at all") to 4 ("very much") except for the items contributing to the GHS/QoL, which are scored 1 ("very poor") to 7 ("excellent"). A linear transformation was applied to the raw scores so that all transformed scores lie between 0 to 100. For the GHS/QoL and 5 functional scales a high score indicates better global health status/functioning and a negative change from baseline indicated less improvement. For the symptom scales, a high score indicates a higher level of symptoms, and a negative change from baseline indicated an improvement in symptoms.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 up to 40 months (Each cycle = 42 days)

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	304		
Units: Score on a Scale				
least squares mean (confidence interval 95%)				
Change from Baseline EORTC QLQ-C30 GHS/QoL	0.46 (-2.715 to 3.642)	-8.54 (-13.004 to -4.084)		
Baseline Change EORTC QLQ-C30 Physical Functioning	-0.27 (-3.014 to 2.473)	-8.86 (-12.517 to -5.196)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With New or Worsened Laboratory Results by National Cancer Institute Common Terminology Criteria for Adverse Event (NCI-CTCAE) Grade

End point title	Number of Participants With New or Worsened Laboratory Results by National Cancer Institute Common Terminology Criteria for Adverse Event (NCI-CTCAE) Grade

End point description:

Laboratory parameters included hematology, electrolytes, chemistry (other), and liver function. Clinically significant abnormalities were determined by the investigator based on NCI-CTCAE Grade where Grade 1 = Mild, Grade 2 = moderate, Grade 3 = severe; Grade 4 = life threatening or disabling; Grade 5 = death. Participants with at least 1 lab abnormality Graded 3/4 in hematology, electrolytes, chemistry (other), or liver function reported. Here 'n' = the number of evaluable participants

End point type	Secondary

End point timeframe:

From date of randomization up to 40 months

End point values	Cemiplimab	Investigator Choice (IC) Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	300	290		
Units: Participants				
Hematology (Grades 3/4)	84	137		
Electrolytes (Grades 3/4)	47	32		
Chemistry (Other) (Grades 3/4)	12	10		
Liver Function (Grades 3/4)	28	23		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose up to 40 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Chemotherapy*

Reporting group description:

Participants received IC of chemotherapy (options listed by class): (1) Antifolate: pemetrexed 500 mg per meter square (mg/m^2) on Day 1; (2) Topoisomerase 1 inhibitor: topotecan 1 mg/m^2 daily for 5 days, starting on Day 1 or irinotecan 100 mg/m^2 weekly (Days 1, 8, 15 and 22), followed by 10 to 14 days rest, for a 42-day (6-week) cycle; (3) Nucleoside analogue: gemcitabine 1000 mg/m^2 on Days 1 and 8; (4) Vinca alkaloid: vinorelbine 30 mg/m^2 IV infusion based on body surface area for Q3W up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.

Reporting group title	Cemiplimab

Reporting group description:

Participants received a fixed dose of 350 milligrams (mg) of cemiplimab intravenous (IV) infusion on Day 1 of every 3 weeks (Q3W) for up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.

Reporting group title	Chemotherapy to Cemiplimab*

Reporting group description:

Treatment until disease progression, unacceptable toxicity, or voluntary withdrawal from the study, or until 96
weeks (16 cycles, each 6 weeks).
Participants received a fixed dose of 350 milligrams (mg) of cemiplimab intravenous (IV) infusion on Day 1 of every 3 weeks (Q3W) for up to 96 weeks (up to 16 cycles of 6 weeks each) or until progression of disease or unacceptable toxicity, voluntary withdrawal from the study.

Serious adverse events	Chemotherapy*	Cemiplimab	Chemotherapy to Cemiplimab*
Total subjects affected by serious adverse events			
subjects affected / exposed	84 / 290 (28.97%)	100 / 300 (33.33%)	1 / 8 (12.50%)
number of deaths (all causes)	249	234	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour associated fever			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Hypotension			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism arterial			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Hypovolaemic shock			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Pyrexia			
subjects affected / exposed	6 / 290 (2.07%)	4 / 300 (1.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	3 / 7	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site thrombosis			

subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Performance status decreased			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hyperpyrexia			
subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	0 / 8 (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
Influenza like illness			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Sudden death			

subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular stent thrombosis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Contrast media allergy			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Vaginal haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	2 / 290 (0.69%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 290 (0.69%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cough			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 290 (0.34%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Haemoptysis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Personality change			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Product issues			
Device occlusion			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Lymphocyte count decreased			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Blood creatinine increased			

subjects affected / exposed	1 / 290 (0.34%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cystitis radiation			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Spinal compression fracture			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device use error			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Transfusion reaction			
subjects affected / exposed	2 / 290 (0.69%)	0 / 300 (0.00%)	0 / 8 (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
Procedural nausea			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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

Autoimmune pericarditis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Pericardial effusion			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	2 / 290 (0.69%)	0 / 300 (0.00%)	0 / 8 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Ischaemic stroke			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 290 (4.83%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	15 / 19	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	6 / 290 (2.07%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	5 / 6	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancytopenia			
subjects affected / exposed	3 / 290 (1.03%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	3 / 290 (1.03%)	0 / 300 (0.00%)	0 / 8 (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
Neutropenia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematochezia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 290 (1.03%)	2 / 300 (0.67%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	2 / 3	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	2 / 290 (0.69%)	0 / 300 (0.00%)	0 / 8 (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
Rectal haemorrhage			
subjects affected / exposed	2 / 290 (0.69%)	0 / 300 (0.00%)	0 / 8 (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

Abdominal pain			
subjects affected / exposed	1 / 290 (0.34%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Diarrhoea			
subjects affected / exposed	3 / 290 (1.03%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Colonic fistula			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Duodenal ulcer			

subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	0 / 8 (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
Nausea			
subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral papule			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal perforation			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Proctalgia			
subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	0 / 8 (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
Proctitis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	0 / 290 (0.00%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			

subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Cholecystitis acute			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Autoimmune hepatitis			
subjects affected / exposed	0 / 290 (0.00%)	4 / 300 (1.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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	3 / 290 (1.03%)	5 / 300 (1.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	2 / 3	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	2 / 290 (0.69%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis haemorrhagic			

subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 290 (0.34%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Renal impairment			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Hydronephrosis			
subjects affected / exposed	0 / 290 (0.00%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	0 / 8 (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
Postrenal failure			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spondylolisthesis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Groin pain			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Arthritis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Muscular weakness			

subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	11 / 290 (3.79%)	15 / 300 (5.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 13	0 / 19	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 290 (1.03%)	5 / 300 (1.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Catheter site infection			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 290 (0.69%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	2 / 290 (0.69%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	3 / 290 (1.03%)	4 / 300 (1.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			

subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected lymphocele			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Neutropenic sepsis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pelvic abscess			
subjects affected / exposed	1 / 290 (0.34%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic shock syndrome streptococcal			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			

subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Staphylococcal infection			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Streptococcal sepsis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Peritonitis			
subjects affected / exposed	1 / 290 (0.34%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 290 (0.00%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			

subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Kidney infection			
subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral rash			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Pyomyositis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 290 (0.00%)	2 / 300 (0.67%)	0 / 8 (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
Staphylococcal sepsis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Stoma site infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Ophthalmic herpes zoster			

subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Diarrhoea infectious			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Urethritis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Hypocalcaemia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Hyperglycaemia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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
Electrolyte imbalance			
subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (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
Decreased appetite			

subjects affected / exposed	0 / 290 (0.00%)	1 / 300 (0.33%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 300 (0.00%)	0 / 8 (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

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

Non-serious adverse events	Chemotherapy*	Cemiplimab	Chemotherapy to Cemiplimab*
Total subjects affected by non-serious adverse events			
subjects affected / exposed	253 / 290 (87.24%)	239 / 300 (79.67%)	4 / 8 (50.00%)
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	16 / 290 (5.52%)	22 / 300 (7.33%)	0 / 8 (0.00%)
occurrences (all)	16	22	0
Fatigue			
subjects affected / exposed	45 / 290 (15.52%)	52 / 300 (17.33%)	0 / 8 (0.00%)
occurrences (all)	81	54	0
Asthenia			
subjects affected / exposed	45 / 290 (15.52%)	35 / 300 (11.67%)	0 / 8 (0.00%)
occurrences (all)	63	37	0
Pyrexia			
subjects affected / exposed	62 / 290 (21.38%)	36 / 300 (12.00%)	2 / 8 (25.00%)
occurrences (all)	117	54	2
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	6 / 290 (2.07%)	15 / 300 (5.00%)	0 / 8 (0.00%)
occurrences (all)	9	16	0

Pelvic pain			
subjects affected / exposed	16 / 290 (5.52%)	13 / 300 (4.33%)	0 / 8 (0.00%)
occurrences (all)	16	14	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	18 / 290 (6.21%)	27 / 300 (9.00%)	0 / 8 (0.00%)
occurrences (all)	22	28	0
Cough			
subjects affected / exposed	21 / 290 (7.24%)	20 / 300 (6.67%)	0 / 8 (0.00%)
occurrences (all)	28	25	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	17 / 290 (5.86%)	20 / 300 (6.67%)	0 / 8 (0.00%)
occurrences (all)	18	21	0
Investigations			
White blood cell count decreased			
subjects affected / exposed	17 / 290 (5.86%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences (all)	35	3	0
Blood creatinine increased			
subjects affected / exposed	16 / 290 (5.52%)	19 / 300 (6.33%)	0 / 8 (0.00%)
occurrences (all)	16	26	0
Aspartate aminotransferase increased			
subjects affected / exposed	19 / 290 (6.55%)	14 / 300 (4.67%)	0 / 8 (0.00%)
occurrences (all)	25	19	0
Alanine aminotransferase increased			
subjects affected / exposed	20 / 290 (6.90%)	14 / 300 (4.67%)	0 / 8 (0.00%)
occurrences (all)	26	14	0
Neutrophil count decreased			
subjects affected / exposed	26 / 290 (8.97%)	3 / 300 (1.00%)	0 / 8 (0.00%)
occurrences (all)	64	7	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	13 / 290 (4.48%)	8 / 300 (2.67%)	1 / 8 (12.50%)
occurrences (all)	38	8	1
Nervous system disorders			

Headache			
subjects affected / exposed	18 / 290 (6.21%)	22 / 300 (7.33%)	0 / 8 (0.00%)
occurrences (all)	19	43	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	15 / 290 (5.17%)	2 / 300 (0.67%)	0 / 8 (0.00%)
occurrences (all)	17	2	0
Neutropenia			
subjects affected / exposed	45 / 290 (15.52%)	9 / 300 (3.00%)	0 / 8 (0.00%)
occurrences (all)	75	11	0
Anaemia			
subjects affected / exposed	128 / 290 (44.14%)	79 / 300 (26.33%)	0 / 8 (0.00%)
occurrences (all)	161	99	0
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	22 / 290 (7.59%)	12 / 300 (4.00%)	0 / 8 (0.00%)
occurrences (all)	24	12	0
Nausea			
subjects affected / exposed	100 / 290 (34.48%)	63 / 300 (21.00%)	0 / 8 (0.00%)
occurrences (all)	175	74	0
Diarrhoea			
subjects affected / exposed	41 / 290 (14.14%)	35 / 300 (11.67%)	1 / 8 (12.50%)
occurrences (all)	60	61	1
Constipation			
subjects affected / exposed	58 / 290 (20.00%)	46 / 300 (15.33%)	1 / 8 (12.50%)
occurrences (all)	64	50	1
Vomiting			
subjects affected / exposed	66 / 290 (22.76%)	49 / 300 (16.33%)	0 / 8 (0.00%)
occurrences (all)	101	65	0
Abdominal pain			
subjects affected / exposed	34 / 290 (11.72%)	28 / 300 (9.33%)	0 / 8 (0.00%)
occurrences (all)	52	31	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	15 / 290 (5.17%)	18 / 300 (6.00%)	0 / 8 (0.00%)
occurrences (all)	15	19	0
Rash			

subjects affected / exposed	19 / 290 (6.55%)	19 / 300 (6.33%)	0 / 8 (0.00%)
occurrences (all)	22	29	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 290 (0.00%)	17 / 300 (5.67%)	0 / 8 (0.00%)
occurrences (all)	0	17	0
Hyperthyroidism			
subjects affected / exposed	0 / 290 (0.00%)	9 / 300 (3.00%)	1 / 8 (12.50%)
occurrences (all)	0	9	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	8 / 290 (2.76%)	18 / 300 (6.00%)	0 / 8 (0.00%)
occurrences (all)	9	20	0
Arthralgia			
subjects affected / exposed	8 / 290 (2.76%)	33 / 300 (11.00%)	0 / 8 (0.00%)
occurrences (all)	11	38	0
Back pain			
subjects affected / exposed	28 / 290 (9.66%)	33 / 300 (11.00%)	0 / 8 (0.00%)
occurrences (all)	29	37	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	18 / 290 (6.21%)	27 / 300 (9.00%)	0 / 8 (0.00%)
occurrences (all)	25	36	0
Subcutaneous abscess			
subjects affected / exposed	0 / 290 (0.00%)	0 / 300 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	46 / 290 (15.86%)	46 / 300 (15.33%)	0 / 8 (0.00%)
occurrences (all)	55	49	0
Hyperglycaemia			
subjects affected / exposed	16 / 290 (5.52%)	4 / 300 (1.33%)	0 / 8 (0.00%)
occurrences (all)	21	4	0
Hypokalaemia			
subjects affected / exposed	17 / 290 (5.86%)	22 / 300 (7.33%)	0 / 8 (0.00%)
occurrences (all)	20	23	0

Hypoalbuminaemia subjects affected / exposed occurrences (all)	19 / 290 (6.55%) 19	23 / 300 (7.67%) 26	0 / 8 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 August 2018	Global Amendment 4
08 March 2019	Global Amendment 5
27 May 2020	Global Amendment 6
14 April 2021	Global Amendment 7

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported