



Clinical trial results:

A Multicenter, Open-label, Randomized, Phase 3 Trial to Compare the Efficacy and Safety of Lenvatinib in Combination With Pembrolizumab Versus Treatment of Physician's Choice in Participants With Advanced Endometrial Cancer

Summary

EudraCT number	2017-004387-35
Trial protocol	FR ES IE GB PL IT
Global end of trial date	26 February 2025

Results information

Result version number	v2 (current)
This version publication date	25 March 2026
First version publication date	06 March 2026
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	3475-775
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03517449
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Merck Sharp & Dohme LLC, Clinical Trials Disclosure, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.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	26 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2022
Global end of trial reached?	Yes
Global end of trial date	26 February 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study of pembrolizumab (MK-3475, KEYTRUDA®) in combination with lenvatinib (E7080) versus treatment of physician's choice (doxorubicin or paclitaxel) for the treatment of advanced endometrial cancer. Participants will be randomly assigned to receive either pembrolizumab and lenvatinib or treatment of physician's choice. The primary study hypothesis is that pembrolizumab in combination with lenvatinib prolongs progression free survival (PFS) and overall survival (OS) when compared to treatment of physician's choice.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2018
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: 23
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Brazil: 37
Country: Number of subjects enrolled	Canada: 58
Country: Number of subjects enrolled	Colombia: 22
Country: Number of subjects enrolled	France: 70
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Italy: 60
Country: Number of subjects enrolled	Japan: 104
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Poland: 27
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	Spain: 38

Country: Number of subjects enrolled	Taiwan: 22
Country: Number of subjects enrolled	Türkiye: 46
Country: Number of subjects enrolled	United Kingdom: 39
Country: Number of subjects enrolled	United States: 114
Worldwide total number of subjects	827
EEA total number of subjects	210

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)	410
From 65 to 84 years	415
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 167 investigative sites in Argentina, Australia, Brazil, Canada, Colombia, France, Germany, Ireland, Israel, Italy, Japan, Korea, Mexico, New Zealand, Poland, Russia, Spain, Taiwan, Turkey, United Kingdom and the United States

Pre-assignment

Screening details:

A total of 1178 participants were screened, of which 351 were screen failures and 827 were enrolled and randomized, out of which 794 participants were 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
Arm title	Lenvatinib 20 mg + Pembrolizumab 200 mg

Arm description:

Participants with Endometrial cancer (EC) received lenvatinib 20 milligrams (mg) orally, once daily, plus pembrolizumab 200 mg intravenously, every 3 weeks in each 21-day cycle. Participants continued to receive treatment until disease progression, development of unacceptable toxicity, withdrawal of consent, completion of 35 treatments (approximately 2 years) with pembrolizumab, or sponsor termination of the study

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA® MK-3475
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg administered by IV infusion on Day 1 of each 21-day cycle

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	LENVIMA®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20 mg administered orally (PO) once daily (QD) during each 21-day cycle

Arm title	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
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Arm description:

Participants with EC received either doxorubicin 60 milligrams per square meter (mg/m²) intravenously, every 3 weeks, in each 21-day treatment cycle, or paclitaxel 80 mg/m² intravenously, weekly (3 weeks on/1 week off), in each 28-day treatment cycle. Participants continued to receive treatment until a lifetime cumulative dose of 500 mg/m² doxorubicin, a maximum dose of paclitaxel per standard of care, or until disease progression, development of unacceptable toxicity, withdrawal of consent, or sponsor termination of the study.

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

Dosage and administration details:

60 mg/m² administered by IV on Day 1 of each 21-day cycle

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	TAXOL®
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m² administered by IV on a 28-day cycle: 3 weeks receiving paclitaxel once a week and 1 week not receiving paclitaxel

Number of subjects in period 1	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
Started	411	416
Completed	411	416

Baseline characteristics

Reporting groups

Reporting group title	Lenvatinib 20 mg + Pembrolizumab 200 mg
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Reporting group description:

Participants with Endometrial cancer (EC) received lenvatinib 20 milligrams (mg) orally, once daily, plus pembrolizumab 200 mg intravenously, every 3 weeks in each 21-day cycle. Participants continued to receive treatment until disease progression, development of unacceptable toxicity, withdrawal of consent, completion of 35 treatments (approximately 2 years) with pembrolizumab, or sponsor termination of the study

Reporting group title	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
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Reporting group description:

Participants with EC received either doxorubicin 60 milligrams per square meter (mg/m²) intravenously, every 3 weeks, in each 21-day treatment cycle, or paclitaxel 80 mg/m² intravenously, weekly (3 weeks on/1 week off), in each 28-day treatment cycle. Participants continued to receive treatment until a lifetime cumulative dose of 500 mg/m² doxorubicin, a maximum dose of paclitaxel per standard of care, or until disease progression, development of unacceptable toxicity, withdrawal of consent, or sponsor termination of the study.

Reporting group values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel	Total
Number of subjects	411	416	827
Age Categorical Units: Participants			
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)	206	204	410
From 65-84 years	205	210	415
85 years and over	0	2	2
Age Continuous Units: years			
arithmetic mean	63.2	63.8	
standard deviation	± 9.1	± 9.2	-
Gender Categorical Units: Participants			
Female	411	416	827
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	59	73	132
Not Hispanic or Latino	309	288	597
Unknown or Not Reported	43	55	98
Race (NIH/OMB) Units: Subjects			
Asian	85	92	177

Black Or African American	17	14	31
White	261	247	508
Unknown or Not Reported	36	43	79
More than one race	7	13	20
American Indian or Alaska Native	4	7	11
Native Hawaiian or Other Pacific Islander	1	0	1
Eastern Cooperative Oncology Group (ECOG) performance status			
Units: Subjects			
0 = Fully active; no performance restrictions	246	241	487
1 = Limited activity, ambulant, can-do light work	165	175	340
Prior history of pelvic radiation			
Units: Subjects			
Yes	176	187	363
No	235	229	464
Geographic region			
Participants from region 1 were included from Europe,USA,Canada,Australia,New Zealand,Israel. Participants from region 2 were included from rest of the world.			
Units: Subjects			
Region 1	234	240	474
Region 2	177	176	353
Mismatch repair (MMR) status			
Units: Subjects			
proficient MMR (pMMR)	346	351	697
deficient (dMMR)	65	65	130

End points

End points reporting groups

Reporting group title	Lenvatinib 20 mg + Pembrolizumab 200 mg
Reporting group description: Participants with Endometrial cancer (EC) received lenvatinib 20 milligrams (mg) orally, once daily, plus pembrolizumab 200 mg intravenously, every 3 weeks in each 21-day cycle. Participants continued to receive treatment until disease progression, development of unacceptable toxicity, withdrawal of consent, completion of 35 treatments (approximately 2 years) with pembrolizumab, or sponsor termination of the study	
Reporting group title	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
Reporting group description: Participants with EC received either doxorubicin 60 milligrams per square meter (mg/m ²) intravenously, every 3 weeks, in each 21-day treatment cycle, or paclitaxel 80 mg/m ² intravenously, weekly (3 weeks on/1 week off), in each 28-day treatment cycle. Participants continued to receive treatment until a lifetime cumulative dose of 500 mg/m ² doxorubicin, a maximum dose of paclitaxel per standard of care, or until disease progression, development of unacceptable toxicity, withdrawal of consent, or sponsor termination of the study.	

Primary: Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) Based on Blinded Independent Central Review (BICR) in mismatch repair proficient (pMMR) Participants

End point title	Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) Based on Blinded Independent Central Review (BICR) in mismatch repair proficient (pMMR) Participants
End point description: PFS was defined as the time from the date of randomization to the date of the first documentation of disease progression, as determined by Blinded Independent Central Review (BICR) per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 or death due to any cause (whichever occurred first). Disease progression was defined as at least 20 percent (%) increase (including an absolute increase of at least 5 millimeter [mm]) in the sum of diameter of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. PFS was estimated and analyzed using Kaplan-Meier method. Analysis population consisted of ITT (intent to treat) population which included all randomized participants.	
End point type	Primary
End point timeframe: Up to approximately 27 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	351		
Units: Months				
median (confidence interval 95%)	6.6 (5.6 to 7.4)	3.8 (3.6 to 5.0)		

Statistical analyses

Statistical analysis title	PFS Hazard Ratio in pMMR Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 ^[1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.72

Notes:

[1] - One-sided p-value based on log-rank test stratified by ECOG performance status, geographic region, and prior history of pelvic radiation.

Primary: PFS per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) Based on BICR in All-comer Participants

End point title	PFS per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) Based on BICR in All-comer Participants
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End point description:

PFS was defined as the time from the date of randomization to the date of the first documentation of disease progression, as determined by Blinded Independent Central Review (BICR) per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 or death due to any cause (whichever occurred first). Disease progression was defined as at least 20 percent (%) increase (including an absolute increase of at least 5 millimeter [mm]) in the sum of diameter of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. PFS was estimated and analyzed using Kaplan-Meier method. Analysis population consisted of ITT population which included all randomized participants.

End point type	Primary
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End point timeframe:

Up to approximately 27 months

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	416		
Units: Months				
median (confidence interval 95%)	7.2 (5.7 to 7.6)	3.8 (3.6 to 4.2)		

Statistical analyses

Statistical analysis title	PFS Hazard Ratio in All-Comer Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
Number of subjects included in analysis	827
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 ^[2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.66

Notes:

[2] - One-sided p-value based on log-rank test stratified by ECOG performance status, geographic region, and prior history of pelvic radiation.

Primary: Overall Survival (OS) in pMMR Participants

End point title	Overall Survival (OS) in pMMR Participants
End point description:	OS was defined as the time from the date of randomization to the date of death due to any cause. Participants who were lost to follow-up and those who were alive at the date of data cut-off were censored at the date the participant was last known alive, or date of data cut-off, whichever occurred first. Analysis population consisted of ITT population which included all randomized participants.
End point type	Primary
End point timeframe:	Up to approximately 43 months

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	351		
Units: Months				
median (confidence interval 95%)	18.0 (14.9 to 20.5)	12.2 (11.0 to 14.1)		

Statistical analyses

Statistical analysis title	OS Hazard Ratio in pMMR Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel

Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 ^[3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.83

Notes:

[3] - One-sided p-value based on log-rank test stratified by ECOG performance status, geographic region, and prior history of pelvic radiation.

Primary: OS in All-Comer Participants

End point title	OS in All-Comer Participants
End point description:	
OS was defined as the time from the date of randomization to the date of death due to any cause. Participants who were lost to follow-up and those who were alive at the date of data cut-off were censored at the date the participant was last known alive, or date of data cut-off, whichever occurred first. Analysis population consisted of ITT population which included all randomized participants.	
End point type	Primary
End point timeframe:	
Up to approximately 43 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	416		
Units: Months				
number (confidence interval 95%)	18.7 (15.6 to 21.3)	11.9 (10.7 to 13.3)		

Statistical analyses

Statistical analysis title	OS Hazard Ratio in All-comer Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel

Number of subjects included in analysis	827
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 ^[4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.77

Notes:

[4] - One-sided p-value based on log-rank test stratified by ECOG performance status, geographic region, and prior history of pelvic radiation.

Secondary: Objective Response Rate (ORR) in pMMR Participants

End point title	Objective Response Rate (ORR) in pMMR Participants
End point description:	
ORR was defined as the percentage of participants who had best overall response of either complete response (CR) or partial response (PR) as determined by BICR per RECIST 1.1. CR was defined as the disappearance of all target and non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis to less than (<) 10mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Analysis population consisted of ITT population which included all randomized participants.	
End point type	Secondary
End point timeframe:	
Up to approximately 80 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	351		
Units: Percentage of participants				
number (confidence interval 95%)	30.3 (25.5 to 35.5)	15.1 (11.5 to 19.3)		

Statistical analyses

Statistical analysis title	ORR Percentage Difference: pMMR Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel

Number of subjects included in analysis	697
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	15.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.1
upper limit	21.4

Secondary: ORR in All-Comer Participants

End point title	ORR in All-Comer Participants
End point description:	
<p>ORR was defined as the percentage of participants who had best overall response of either complete response (CR) or partial response (PR) as determined by BICR per RECIST 1.1. CR was defined as the disappearance of all target and non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis to less than (<) 10mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Analysis population consisted of ITT population which included all randomized participants.</p>	
End point type	Secondary
End point timeframe:	
Up to approximately 80 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	416		
Units: Percentage of Participants				
number (confidence interval 95%)	31.9 (27.4 to 36.6)	14.7 (11.4 to 18.4)		

Statistical analyses

Statistical analysis title	ORR Percentage Difference: All-Comer Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel

Number of subjects included in analysis	827
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.5
upper limit	22.9

Secondary: Change from Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) in pMMR Participants

End point title	Change from Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) in pMMR Participants
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End point description:

EORTC QLQ-C30 was a questionnaire which included 30 questions that rates the overall quality of life in cancer participants. The first 28 questions use a 4-point scale (1=not at all to 4=very much) for evaluating function (physical, role, social, cognitive, emotional), symptoms (diarrhea, fatigue, dyspnea, appetite loss, insomnia, nausea/vomiting, constipation, and pain) and financial difficulties. The last 2 questions use a 7-point scale (1=very poor to 7=excellent) to evaluate overall health and quality of life. Scores are transformed to a range of 0 to 100 using a standard EORTC algorithm. A high score for a functional scale represents a high/healthy level of functioning, a high score for the global health status/quality of life (QoL) represents a high QoL, but a high score for a symptom scale/item represents a high level of symptomatology/problem. Analysis population consisted of ITT population which included all randomized participants.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):D oxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	327	310		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-6.80 (-9.43 to -4.17)	-7.96 (-10.86 to -5.05)		

Statistical analyses

Statistical analysis title	Difference in LS mean in pMMR Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
Number of subjects included in analysis	637
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5316
Method	cLDA model
Parameter estimate	Difference in LS Means
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.49
upper limit	4.81

Secondary: Change from Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) in All-Comer Participants

End point title	Change from Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) in All-Comer Participants
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End point description:

EORTC QLQ-C30 was a questionnaire which included 30 questions that rates the overall quality of life in cancer participants. The first 28 questions use a 4-point scale (1=not at all to 4=very much) for evaluating function (physical, role, social, cognitive, emotional), symptoms (diarrhea, fatigue, dyspnea, appetite loss, insomnia, nausea/vomiting, constipation, and pain) and financial difficulties. The last 2 questions use a 7-point scale (1=very poor to 7=excellent) to evaluate overall health and quality of life. Scores are transformed to a range of 0 to 100 using a standard EORTC algorithm. A high score for a functional scale represents a high/healthy level of functioning, a high score for the global health status/quality of life (QoL) represents a high QoL, but a high score for a symptom scale/item represents a high level of symptomatology/problem. Analysis population consisted of ITT population which included all randomized participants.

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386	363		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-5.97 (-8.36 to -3.58)	-6.98 (-9.63 to -4.33)		

Statistical analyses

Statistical analysis title	Difference in LS mean in All-comer Participants
Comparison groups	Lenvatinib 20 mg + Pembrolizumab 200 mg v Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel
Number of subjects included in analysis	749
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.546
Method	cLDA model
Parameter estimate	Difference in LS Means
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.28
upper limit	4.31

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Immune-Related Adverse Events (irAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Immune-Related Adverse Events (irAEs)
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End point description:

TEAEs were AEs that occurred (or worsened, if present at baseline) after the first dose of study drug through 28 days after the last dose. An AE was any untoward medical occurrence in a participant temporally associated with use of study treatment, whether or not related to the treatment. An SAE was any untoward medical occurrence at any dose that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, or was a congenital anomaly/birth defect. An irAE was any unfavorable and unintended immune-related sign, symptom, or disease (new or worsening) temporally associated with study therapy, regardless of whether a causal relationship with the therapy could be determined. The analysis population included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary
End point timeframe:	
Up to approximately 77 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):Doxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	406	388		
Units: Participants	237	121		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Discontinued Study Treatment Due to a TAE in pMMR Participants

End point title	Number of Participants Who Discontinued Study Treatment Due to a TAE in pMMR Participants
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End point description:

TEAEs was defined as those AEs that occurred (or worsened, if present at Baseline) after the first dose of study drug through 30 days after the last dose of study drug. An AE was defined as any untoward medical occurrence in a participants or clinical study participant temporally associated with the use of study treatment, whether or not considered related to the study treatment. Safety analysis population included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 77 months

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):D oxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	325		
Units: Participants	140	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Discontinued Study Treatment Due to a TAE in All-Comer Participants

End point title	Number of Participants Who Discontinued Study Treatment Due to a TAE in All-Comer Participants
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End point description:

TEAEs was defined as those AEs that occurred (or worsened, if present at Baseline) after the first dose of study drug through 30 days after the last dose of study drug. An AE was defined as any untoward medical occurrence in a participants or clinical study participant temporally associated with the use of study treatment, whether or not considered related to the study treatment. Safety analysis population included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 77 months

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):D oxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	406	388		
Units: Participants	180	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure Due to Toxicity in pMMR Participants

End point title	Time to Treatment Failure Due to Toxicity in pMMR Participants
End point description:	
Time to treatment failure due to toxicity was defined as the time from the date of randomization to the date a participant discontinued study treatment due to TEAEs. Safety analysis population included all randomized participants who received at least 1 dose of study treatment.	
End point type	Secondary
End point timeframe:	
Up to approximately 77 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):D oxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	325		
Units: Months				
geometric mean (standard deviation)	429.6 (± 491.6)	260.1 (± 356.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure Due to Toxicity in All-Comer Participants

End point title	Time to Treatment Failure Due to Toxicity in All-Comer Participants
End point description:	
Time to treatment failure due to toxicity was defined as the time from the date of randomization to the date a participant discontinued study treatment due to TEAEs. Safety analysis population included all randomized participants who received at least 1 dose of study treatment.	
End point type	Secondary
End point timeframe:	
Up to approximately 77 months	

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg	Treatment of Physician's Choice(TPC):D oxorubicin or Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	406	388		
Units: Months				
geometric mean (standard deviation)	456.5 (± 520.6)	259.7 (± 369.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Lenvatinib Versus Time in All-Comer Participants

End point title	Plasma Concentration of Lenvatinib Versus Time in All-Comer Participants ^[5]
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End point description:

Pharmacokinetic (PK) samples were collected and analyzed using a population PK approach to estimate PK parameters. Individual predicted plasma concentration of lenvatinib was then derived from the PK model. Analysis population included all participants who have received at least 1 dose of study treatment with documented dosing history in the lenvatinib plus pembrolizumab arm and have measurable plasma levels of lenvatinib.

End point type	Secondary
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End point timeframe:

Cycle 1 day 1 0.5-4 hours (h), 6-10 postdose; Cycle 1 day 15 predose; Cycle 1 day 15 2-12h postdose. Cycle 2 day 1 predose, 0.5-4h, 6-10 h. Each cycle is 21 days.

Notes:

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

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	403			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0.5-4h Post-dose (N=317)	152 (± 181)			
Cycle 1 Day 1, 6-10 h Post-dose (N=345)	258 (± 124)			
Cycle 1 Day 15, Pre-dose (N=332)	89.1 (± 69.6)			
Cycle 1 Day 15, 2-12 h Post-dose (N=316)	310 (± 218)			
Cycle 2 Day 1, Pre-dose (N=300)	67.2 (± 74.7)			
Cycle 2 Day 1, 0.5-4h (N=342)	151 (± 155)			

Cycle 2 Day 1, 6-10 h (N=283)	258 (\pm 138)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Lenvatinib Versus Time in pMMR Participants

End point title	Plasma Concentration of Lenvatinib Versus Time in pMMR Participants ^[6]
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End point description:

Pharmacokinetic (PK) samples were collected and analyzed using a population PK approach to estimate PK parameters. Individual predicted plasma concentration of lenvatinib was then derived from the PK model. Analysis population included all participants who have received at least 1 dose of study treatment with documented dosing history in the lenvatinib plus pembrolizumab arm and have measurable plasma levels of lenvatinib.

End point type	Secondary
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End point timeframe:

Cycle 1 day 1 0.5-4 h, 6-10 postdose; Cycle 1 day 15 predose; Cycle 1 day 15 2-12h postdose. Cycle 2 day 1 predose, 0.5-4h, 6-10 h. Each cycle is 21 days.

Notes:

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

Justification: No statistical analyses for this end point

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, 0.5-4 h Post-dose (N=50)	140 (\pm 180)			
Cycle 1 Day 1, 6-10 h Post-dose (N=51)	283 (\pm 136)			
Cycle 1 Day 15, Pre-dose (N=51)	93.8 (\pm 61.4)			
Cycle 1 Day 15, 2-12 h Post-dose (N=51)	335 (\pm 256)			
Cycle 2 Day 1, Pre-dose (N=44)	67.9 (\pm 60.9)			
Cycle 2 Day 1, 0.5-4 h (N=58)	153 (\pm 127)			
Cycle 2 Day 1, 6-10 h (N=41)	278 (\pm 132)			

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Apparent Total Clearance (CL/F) for Lenvatinib

End point title	Model Predicted Apparent Total Clearance (CL/F) for
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End point description:

Sparse pharmacokinetic (PK) samples were collected and analyzed using a population PK approach to estimate PK parameters. Individual predicted CL/F for lenvatinib was then derived from the PK model. The data was collected and analyzed for lenvatinib plus pembrolizumab arm only. The population pharmacokinetic analysis set includes all the participants who have received at least 1 dose of study treatment with documented dosing history in the lenvatinib plus pembrolizumab arm, and have measurable plasma levels of lenvatinib. Here "overall number of participants analyzed" signifies participants who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Cycle 1 Day 1: 0.5-10 hours post-dose; Cycle 1 Day 15: 0-12 hours post-dose; Cycle 2 Day 1: 0.5-10 hours post-dose (each cycle length=21 days)

Notes:

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

Justification: No statistical analyses for this end point

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	403			
Units: liter per hour (L/h)				
geometric mean (standard deviation)	4.69 (± 1.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Area Under the Plasma Drug Concentration-time Curve (AUC) for Lenvatinib

End point title	Model Predicted Area Under the Plasma Drug Concentration-time Curve (AUC) for Lenvatinib ^[8]
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End point description:

Sparse PK samples were collected and analyzed using a population PK approach to estimate PK parameters. Individual predicted AUC for lenvatinib was then derived from the PK model. The data was collected and analyzed for lenvatinib plus pembrolizumab arm only. The population pharmacokinetic analysis set includes all the participants who have received at least 1 dose of study treatment with documented dosing history in the lenvatinib plus pembrolizumab arm, and have measurable plasma levels of lenvatinib. Here "overall number of participants analyzed" signifies participants who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Cycle 1 Day 1: 0.5-10 hours post-dose; Cycle 1 Day 15: 0-12 hours post-dose; Cycle 2 Day 1: 0.5-10 hours post-dose (each cycle length=21 days)

Notes:

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

Justification: No statistical analyses for this end point

End point values	Lenvatinib 20 mg + Pembrolizumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	403			
Units: nanogram*hourper milliliter (ng*h/mL)				
median (standard deviation)	4134 (± 1350)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 79 months

Adverse event reporting additional description:

All-cause mortality was reported on all randomized participants. AEs were reported on participants who received at least 1 dose of treatment. MedDRA preferred terms Neoplasm progression, Malignant neoplasm progression & Disease progression not related to drug were excluded.

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	First Course: Lenvatinib + Pembrolizumab
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Reporting group description:

Participants with Endometrial cancer (EC) received lenvatinib 20 milligrams (mg) orally, once daily, plus pembrolizumab 200 mg intravenously, every 3 weeks in each 21-day cycle. Participants continued to receive treatment until disease progression, development of unacceptable toxicity, withdrawal of consent, completion of 35 treatments (approximately 2 years) with pembrolizumab, or sponsor termination of the study

Reporting group title	TPC Crossover
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Reporting group description:

Eligible participants who completed the first course of either doxorubicin 60 milligrams per square meter (mg/m²) intravenously, every 3 weeks, in each 21-day treatment cycle, or paclitaxel 80 mg/m² intravenously, weekly (3 weeks on/1 week off), in each 28-day treatment cycle and eligible participants continued to receive treatment until a lifetime cumulative dose of 500 mg/m² doxorubicin, a maximum dose of paclitaxel per standard of care or who had Stable disease (SD) or partial response (PR) or had attained complete response (CR), but experienced radiologic progression of disease (PD) initiated treatment with pembrolizumab and lenvatinib at investigators discretion at the same dose and schedule at lenvatinib 20 mg orally, once daily, plus pembrolizumab 200 mg intravenously, every 3 weeks in each 21-day cycle upto 17 cycles (upto ~1 year)

Reporting group title	Second Course: Lenvatinib + Pembrolizumab
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Reporting group description:

Eligible participants who completed the first course of up to 35 administrations of pembrolizumab (~2 years) and lenvatinib (~2years) or who had Stable disease (SD) or partial response (PR) or had attained complete response (CR), but experienced radiologic progression of disease (PD) initiated a second course of pembrolizumab and lenvatinib at investigators discretion at the same dose and schedule at lenvatinib 20 mg orally, once daily, plus pembrolizumab 200 mg intravenously, every 3 weeks in each 21-day cycle upto 17 cycles (upto ~1 year)

Reporting group title	First Course: TPC Doxorubicin or Paclitaxel
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Reporting group description:

Participants with EC received either doxorubicin 60 milligrams per square meter (mg/m²) intravenously, every 3 weeks, in each 21-day treatment cycle, or paclitaxel 80 mg/m² intravenously, weekly (3 weeks on/1 week off), in each 28-day treatment cycle. Participants continued to receive treatment until a lifetime cumulative dose of 500 mg/m² doxorubicin, a maximum dose of paclitaxel per standard of care, or until disease progression, development of unacceptable toxicity, withdrawal of consent, or sponsor termination of the study.

Serious adverse events	First Course: Lenvatinib + Pembrolizumab	TPC Crossover	Second Course: Lenvatinib + Pembrolizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	237 / 406 (58.37%)	1 / 6 (16.67%)	4 / 21 (19.05%)

number of deaths (all causes)	317	1	8
number of deaths resulting from adverse events	26	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myelomonocytic leukaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cholangiocarcinoma			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Malignant melanoma in situ			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Vascular disorders			
Aortic thrombosis			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Arteriosclerosis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic venous thrombosis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	17 / 406 (4.19%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	17 / 17	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Hypovolaemic shock			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Jugular vein thrombosis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Vasculitis			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Thrombosis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Assisted suicide			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
General physical health deterioration			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	5 / 406 (1.23%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 0
Device related thrombosis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue				
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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	
Catheter site inflammation				
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Generalised oedema				
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Hyperpyrexia				
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Malaise				
subjects affected / exposed	0 / 406 (0.00%)	1 / 6 (16.67%)	0 / 21 (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	
Mucosal inflammation				
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	
Oedema peripheral				
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	
Perforated ulcer				

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Pyrexia			
subjects affected / exposed	8 / 406 (1.97%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	4 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic shock			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Anaphylactic reaction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Female genital tract fistula			
subjects affected / exposed	4 / 406 (0.99%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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

Vaginal haemorrhage			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Aspiration			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	4 / 406 (0.99%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung opacity			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Pleural effusion			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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

Pneumonitis			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Respiratory distress			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Delirium			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Anxiety			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Product issues			

Device dislocation			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
ECG signs of myocardial ischaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatic enzyme increased			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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			
Craniocerebral injury			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Fall			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Femur fracture			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 radiation			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Postoperative ileus			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Skull fractured base			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Subdural haematoma			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
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 procedure complication subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Radius fracture subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Acute myocardial infarction subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Angina pectoris subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 coronary syndrome subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bundle branch block left subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cardiac failure			

subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Left ventricular dysfunction			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Right ventricular dysfunction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Toxic cardiomyopathy			

subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Ventricular fibrillation			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cerebral infarction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis autoimmune			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Encephalopathy			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Haemorrhagic stroke			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Neuralgia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Middle cerebral artery stroke			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Migraine			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Myasthenia gravis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Nervous system disorder			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Headache			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic neuritis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Seizure			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Tremor			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophilia			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
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	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Leukocytosis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Thrombotic microangiopathy			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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			
Iridocyclitis			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 406 (0.99%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Anal fissure			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Constipation			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Colitis			
subjects affected / exposed	7 / 406 (1.72%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	7 / 7	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Colonic fistula			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Diarrhoea			

subjects affected / exposed	10 / 406 (2.46%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	6 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Duodenal obstruction			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
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 erosive			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Enterocolitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Fistula of small intestine			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Gastritis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Enteritis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Gastrointestinal perforation			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Gastrointestinal toxicity			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	4 / 406 (0.99%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal fistula			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Intestinal obstruction			
subjects affected / exposed	5 / 406 (1.23%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			

subjects affected / exposed	4 / 406 (0.99%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ischaemic enteritis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated pancreatitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Mechanical ileus			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Nausea			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Proctalgia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Proctitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Malignant gastrointestinal obstruction			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Small intestinal obstruction			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Large intestine perforation			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Lower gastrointestinal perforation			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Rectal perforation			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Stomatitis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Umbilical hernia			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	9 / 406 (2.22%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	7 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Biliary obstruction			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	8 / 406 (1.97%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	3 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	4 / 406 (0.99%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminaemia			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disease			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Hepatic function abnormal			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Hepatic failure			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cholelithiasis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cholecystitis acute			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Liver injury			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 disorder			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Toxic skin eruption			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Rash macular			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Stasis dermatitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Stevens-Johnson syndrome			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Pyoderma gangrenosum			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Umbilical haemorrhage			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
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			
Haematuria			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	9 / 406 (2.22%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	4 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Haemorrhage urinary tract			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Nephrolithiasis			

subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
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 disorder			
subjects affected / exposed	0 / 406 (0.00%)	1 / 6 (16.67%)	0 / 21 (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
Renal injury			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Urinary tract obstruction			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Urogenital fistula			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Renal failure			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	3 / 406 (0.74%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenocorticotrophic hormone deficiency			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Hypophysitis			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Hypothyroidism			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Hyperthyroidism			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Arthritis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Back pain			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Pathological fracture			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Myalgia			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Myositis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Pain in extremity			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Bone pain			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Appendicitis perforated			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Appendicitis			

subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Escherichia bacteraemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Encephalitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 infectious			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Bacterial infection			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Biliary tract infection			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Device related infection			

subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Cystitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Cellulitis			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Bacteraemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Gastroenteritis norovirus			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 Escherichia coli			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Omphalitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Oesophageal candidiasis			

subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Meningitis bacterial			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Hepatitis A			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 fistula			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic abscess			

subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	6 / 406 (1.48%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Psoas abscess			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Pyelonephritis			
subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal abscess			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	6 / 406 (1.48%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sialoadenitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Sinusitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 bacteraemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Tonsillitis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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 respiratory tract infection			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Urosepsis			

subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vaginal abscess			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Vaginal infection			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	14 / 406 (3.45%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 16	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Decreased appetite			
subjects affected / exposed	9 / 406 (2.22%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	7 / 9	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	5 / 406 (1.23%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			

subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Hypercalcaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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	2 / 406 (0.49%)	0 / 6 (0.00%)	0 / 21 (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
Hypochloraemia			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Type 1 diabetes mellitus			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Hypomagnesaemia			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (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
Hyponatraemia			

subjects affected / exposed	2 / 406 (0.49%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 406 (0.00%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	3 / 406 (0.74%)	0 / 6 (0.00%)	0 / 21 (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
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 406 (0.25%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	First Course: TPC Doxorubicin or Paclitaxel		
Total subjects affected by serious adverse events			
subjects affected / exposed	121 / 388 (31.19%)		
number of deaths (all causes)	362		
number of deaths resulting from adverse events	20		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myelomonocytic leukaemia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangiocarcinoma			

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma in situ			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Plasma cell myeloma			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic thrombosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arteriosclerosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pelvic venous thrombosis			

subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jugular vein thrombosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vasculitis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Assisted suicide			

subjects affected / exposed	0 / 388 (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	2 / 388 (0.52%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Condition aggravated			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Device related thrombosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Catheter site inflammation			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Generalised oedema			

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperpyrexia			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	0 / 388 (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	2 / 388 (0.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Oedema peripheral			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Perforated ulcer			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaphylactic shock			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaphylactic reaction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Female genital tract fistula			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine haemorrhage			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Aspiration				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Dyspnoea				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	5 / 388 (1.29%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	1 / 1			
Epistaxis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung opacity				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Blood creatinine increased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ECG signs of myocardial ischaemia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ejection fraction decreased			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lipase increased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Fall				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis radiation				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative ileus				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skull fractured base				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vascular procedure complication				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				

subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute coronary syndrome			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bundle branch block left			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	1 / 1		
Cardiac failure congestive			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Myocarditis			

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Left ventricular dysfunction			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiogenic shock			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 2		
Pericardial effusion			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Right ventricular dysfunction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic cardiomyopathy			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Stress cardiomyopathy			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			

subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular fibrillation			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalitis autoimmune			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			

subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuralgia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Middle cerebral artery stroke				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myasthenia gravis				
subjects affected / exposed	0 / 388 (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 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Optic neuritis				

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 388 (2.32%)		
occurrences causally related to treatment / all	7 / 9		
deaths causally related to treatment / all	0 / 0		
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	16 / 388 (4.12%)		
occurrences causally related to treatment / all	16 / 17		
deaths causally related to treatment / all	0 / 0		
Neutrophilia			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			

subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	8 / 388 (2.06%)		
occurrences causally related to treatment / all	7 / 8		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombotic microangiopathy			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			

subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colonic fistula				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	3 / 388 (0.77%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	3 / 388 (0.77%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal obstruction				

subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fistula of small intestine				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal perforation				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal toxicity				

subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestinal obstruction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal fistula			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic enteritis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated pancreatitis			

subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mechanical ileus				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctalgia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant gastrointestinal obstruction				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal perforation			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal perforation			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute hepatic failure			

subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Bile duct stone				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary obstruction				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated hepatitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertransaminaemia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatotoxicity				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disease				

subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic function abnormal			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver disorder			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Drug eruption			

subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash macular				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stasis dermatitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stevens-Johnson syndrome				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyoderma gangrenosum				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical haemorrhage				

subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Autoimmune nephritis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage urinary tract			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal disorder			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal injury			

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urogenital fistula			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adrenocorticotrophic hormone deficiency			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypophysitis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypothyroidism			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fistula			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	0 / 388 (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 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Periarthritis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia bacteraemia			

subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary tract infection				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis Escherichia coli				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Omphalitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal candidiasis				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Necrotising fasciitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis bacterial				

subjects affected / exposed	0 / 388 (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 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatitis A				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected fistula				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	4 / 388 (1.03%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	2 / 2			
Postoperative wound infection				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psoas abscess				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal abscess				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	5 / 388 (1.29%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	1 / 3			
Septic shock				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sialoadenitis				

subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal bacteraemia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vaginal abscess				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaginal infection				

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			

subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypochloraemia				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Type 1 diabetes mellitus				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypomagnesaemia				
subjects affected / exposed	0 / 388 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	2 / 388 (0.52%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypophosphataemia				
subjects affected / exposed	1 / 388 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malnutrition				

subjects affected / exposed	0 / 388 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	First Course: Lenvatinib + Pembrolizumab	TPC Crossover	Second Course: Lenvatinib + Pembrolizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	404 / 406 (99.51%)	6 / 6 (100.00%)	20 / 21 (95.24%)
Vascular disorders			
Hypertension			
subjects affected / exposed	255 / 406 (62.81%)	2 / 6 (33.33%)	1 / 21 (4.76%)
occurrences (all)	435	4	2
Hot flush			
subjects affected / exposed	8 / 406 (1.97%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	9	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	99 / 406 (24.38%)	0 / 6 (0.00%)	2 / 21 (9.52%)
occurrences (all)	129	0	3
Pyrexia			
subjects affected / exposed	62 / 406 (15.27%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	99	1	2
Oedema peripheral			
subjects affected / exposed	57 / 406 (14.04%)	0 / 6 (0.00%)	3 / 21 (14.29%)
occurrences (all)	76	0	3

Mucosal inflammation subjects affected / exposed occurrences (all)	54 / 406 (13.30%) 73	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	25 / 406 (6.16%) 35	0 / 6 (0.00%) 0	0 / 21 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	138 / 406 (33.99%) 176	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	14 / 406 (3.45%) 16	1 / 6 (16.67%) 1	1 / 21 (4.76%) 1
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	1 / 406 (0.25%) 1	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	21 / 406 (5.17%) 26	0 / 6 (0.00%) 0	0 / 21 (0.00%) 0
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	7 / 406 (1.72%) 7	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all)	7 / 406 (1.72%) 8	2 / 6 (33.33%) 2	0 / 21 (0.00%) 0
Productive cough subjects affected / exposed occurrences (all)	4 / 406 (0.99%) 4	1 / 6 (16.67%) 1	1 / 21 (4.76%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	25 / 406 (6.16%) 31	0 / 6 (0.00%) 0	1 / 21 (4.76%) 1
Epistaxis subjects affected / exposed occurrences (all)	34 / 406 (8.37%) 39	0 / 6 (0.00%) 0	0 / 21 (0.00%) 0
Dyspnoea exertional			

subjects affected / exposed occurrences (all)	7 / 406 (1.72%) 7	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	50 / 406 (12.32%) 55	0 / 6 (0.00%) 0	3 / 21 (14.29%) 3
Dysphonia subjects affected / exposed occurrences (all)	95 / 406 (23.40%) 114	4 / 6 (66.67%) 4	0 / 21 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	63 / 406 (15.52%) 78	0 / 6 (0.00%) 0	2 / 21 (9.52%) 2
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	14 / 406 (3.45%) 14	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	35 / 406 (8.62%) 38	0 / 6 (0.00%) 0	0 / 21 (0.00%) 0
Initial insomnia subjects affected / exposed occurrences (all)	0 / 406 (0.00%) 0	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Investigations			
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	55 / 406 (13.55%) 81	0 / 6 (0.00%) 0	1 / 21 (4.76%) 2
Blood bilirubin increased subjects affected / exposed occurrences (all)	25 / 406 (6.16%) 30	0 / 6 (0.00%) 0	0 / 21 (0.00%) 0
Blood calcium decreased subjects affected / exposed occurrences (all)	3 / 406 (0.74%) 3	1 / 6 (16.67%) 1	0 / 21 (0.00%) 0
Blood chloride decreased subjects affected / exposed occurrences (all)	4 / 406 (0.99%) 4	1 / 6 (16.67%) 5	0 / 21 (0.00%) 0
Blood cholesterol increased			

subjects affected / exposed	40 / 406 (9.85%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	68	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	23 / 406 (5.67%)	2 / 6 (33.33%)	0 / 21 (0.00%)
occurrences (all)	28	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	89 / 406 (21.92%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	160	0	1
Amylase increased			
subjects affected / exposed	37 / 406 (9.11%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	60	0	0
Alanine aminotransferase increased			
subjects affected / exposed	95 / 406 (23.40%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	160	0	1
Blood creatinine increased			
subjects affected / exposed	49 / 406 (12.07%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	70	2	4
Blood lactate dehydrogenase increased			
subjects affected / exposed	22 / 406 (5.42%)	1 / 6 (16.67%)	1 / 21 (4.76%)
occurrences (all)	30	3	1
Blood magnesium decreased			
subjects affected / exposed	8 / 406 (1.97%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	18	4	0
Blood phosphorus decreased			
subjects affected / exposed	3 / 406 (0.74%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	3	1	0
Blood sodium decreased			
subjects affected / exposed	5 / 406 (1.23%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	9	2	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	54 / 406 (13.30%)	1 / 6 (16.67%)	1 / 21 (4.76%)
occurrences (all)	61	3	1
Blood urea increased			

subjects affected / exposed	6 / 406 (1.48%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	11	2	0
International normalised ratio increased			
subjects affected / exposed	0 / 406 (0.00%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Lipase increased			
subjects affected / exposed	54 / 406 (13.30%)	2 / 6 (33.33%)	3 / 21 (14.29%)
occurrences (all)	86	3	3
Lymphocyte count decreased			
subjects affected / exposed	17 / 406 (4.19%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	28	0	0
Neutrophil count decreased			
subjects affected / exposed	23 / 406 (5.67%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	39	1	0
Platelet count decreased			
subjects affected / exposed	52 / 406 (12.81%)	2 / 6 (33.33%)	0 / 21 (0.00%)
occurrences (all)	96	2	0
Weight decreased			
subjects affected / exposed	147 / 406 (36.21%)	3 / 6 (50.00%)	1 / 21 (4.76%)
occurrences (all)	169	5	1
White blood cell count decreased			
subjects affected / exposed	21 / 406 (5.17%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	29	1	2
White blood cell count increased			
subjects affected / exposed	1 / 406 (0.25%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Taste disorder			
subjects affected / exposed	7 / 406 (1.72%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	8	1	0
Neuropathy peripheral			
subjects affected / exposed	19 / 406 (4.68%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	26	1	0
Headache			

subjects affected / exposed	107 / 406 (26.35%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	154	0	0
Dysgeusia			
subjects affected / exposed	42 / 406 (10.34%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	46	0	0
Dizziness			
subjects affected / exposed	46 / 406 (11.33%)	0 / 6 (0.00%)	2 / 21 (9.52%)
occurrences (all)	54	0	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	115 / 406 (28.33%)	1 / 6 (16.67%)	1 / 21 (4.76%)
occurrences (all)	171	3	1
Lymphopenia			
subjects affected / exposed	26 / 406 (6.40%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	61	1	5
Leukopenia			
subjects affected / exposed	28 / 406 (6.90%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	72	0	3
Thrombocytopenia			
subjects affected / exposed	46 / 406 (11.33%)	2 / 6 (33.33%)	0 / 21 (0.00%)
occurrences (all)	66	3	0
Neutropenia			
subjects affected / exposed	38 / 406 (9.36%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	106	0	3
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	2 / 406 (0.49%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	3 / 406 (0.74%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	3	1	0
Diplopia			
subjects affected / exposed	2 / 406 (0.49%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	96 / 406 (23.65%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	141	1	0
Abdominal discomfort			
subjects affected / exposed	9 / 406 (2.22%)	1 / 6 (16.67%)	1 / 21 (4.76%)
occurrences (all)	10	1	1
Abdominal pain upper			
subjects affected / exposed	57 / 406 (14.04%)	1 / 6 (16.67%)	3 / 21 (14.29%)
occurrences (all)	75	1	3
Nausea			
subjects affected / exposed	212 / 406 (52.22%)	2 / 6 (33.33%)	1 / 21 (4.76%)
occurrences (all)	352	3	2
Intestinal obstruction			
subjects affected / exposed	2 / 406 (0.49%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Haemorrhoids			
subjects affected / exposed	28 / 406 (6.90%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	30	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	31 / 406 (7.64%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	36	0	0
Odynophagia			
subjects affected / exposed	4 / 406 (0.99%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	6	1	0
Dyspepsia			
subjects affected / exposed	31 / 406 (7.64%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	37	0	0
Dry mouth			
subjects affected / exposed	43 / 406 (10.59%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	51	0	0
Diarrhoea			
subjects affected / exposed	223 / 406 (54.93%)	3 / 6 (50.00%)	4 / 21 (19.05%)
occurrences (all)	686	6	5
Constipation			
subjects affected / exposed	116 / 406 (28.57%)	2 / 6 (33.33%)	0 / 21 (0.00%)
occurrences (all)	142	2	0

Gastritis			
subjects affected / exposed	23 / 406 (5.67%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	26	0	0
Vomiting			
subjects affected / exposed	149 / 406 (36.70%)	3 / 6 (50.00%)	2 / 21 (9.52%)
occurrences (all)	337	4	3
Stomatitis			
subjects affected / exposed	79 / 406 (19.46%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	97	0	1
Oral pain			
subjects affected / exposed	21 / 406 (5.17%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	25	0	0
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	2 / 406 (0.49%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Pruritus			
subjects affected / exposed	46 / 406 (11.33%)	2 / 6 (33.33%)	2 / 21 (9.52%)
occurrences (all)	59	2	2
Rash			
subjects affected / exposed	66 / 406 (16.26%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	91	1	2
Rash pruritic			
subjects affected / exposed	4 / 406 (0.99%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	4	1	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	86 / 406 (21.18%)	3 / 6 (50.00%)	0 / 21 (0.00%)
occurrences (all)	98	3	0
Dry skin			
subjects affected / exposed	32 / 406 (7.88%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	37	0	0
Dermatitis			
subjects affected / exposed	9 / 406 (2.22%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	10	1	0
Alopecia			

subjects affected / exposed occurrences (all)	25 / 406 (6.16%) 26	0 / 6 (0.00%) 0	0 / 21 (0.00%) 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	128 / 406 (31.53%)	2 / 6 (33.33%)	4 / 21 (19.05%)
occurrences (all)	275	2	10
Leukocyturia			
subjects affected / exposed	4 / 406 (0.99%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	9	1	0
Dysuria			
subjects affected / exposed	25 / 406 (6.16%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	28	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	238 / 406 (58.62%)	4 / 6 (66.67%)	4 / 21 (19.05%)
occurrences (all)	299	4	5
Hyperthyroidism			
subjects affected / exposed	46 / 406 (11.33%)	1 / 6 (16.67%)	1 / 21 (4.76%)
occurrences (all)	50	1	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	72 / 406 (17.73%)	2 / 6 (33.33%)	0 / 21 (0.00%)
occurrences (all)	98	2	0
Muscle spasms			
subjects affected / exposed	17 / 406 (4.19%)	2 / 6 (33.33%)	0 / 21 (0.00%)
occurrences (all)	23	3	0
Bone pain			
subjects affected / exposed	11 / 406 (2.71%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	13	1	0
Back pain			
subjects affected / exposed	60 / 406 (14.78%)	0 / 6 (0.00%)	5 / 21 (23.81%)
occurrences (all)	76	0	5
Arthralgia			
subjects affected / exposed	137 / 406 (33.74%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	209	2	3
Pain in extremity			

subjects affected / exposed occurrences (all)	55 / 406 (13.55%) 73	3 / 6 (50.00%) 3	1 / 21 (4.76%) 1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	25 / 406 (6.16%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	27	1	2
Tinea infection			
subjects affected / exposed	1 / 406 (0.25%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Respiratory tract infection			
subjects affected / exposed	2 / 406 (0.49%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Oral herpes			
subjects affected / exposed	4 / 406 (0.99%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	6	1	0
COVID-19			
subjects affected / exposed	11 / 406 (2.71%)	2 / 6 (33.33%)	2 / 21 (9.52%)
occurrences (all)	11	2	2
Influenza			
subjects affected / exposed	8 / 406 (1.97%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	8	1	0
Fungal foot infection			
subjects affected / exposed	1 / 406 (0.25%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Cystitis			
subjects affected / exposed	24 / 406 (5.91%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	29	0	0
Cellulitis			
subjects affected / exposed	5 / 406 (1.23%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	5	1	0
Nasopharyngitis			
subjects affected / exposed	17 / 406 (4.19%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	19	0	0
Urinary tract infection			
subjects affected / exposed	106 / 406 (26.11%)	2 / 6 (33.33%)	2 / 21 (9.52%)
occurrences (all)	171	2	2

Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	57 / 406 (14.04%)	1 / 6 (16.67%)	0 / 21 (0.00%)
occurrences (all)	102	1	0
Hyperkalaemia			
subjects affected / exposed	20 / 406 (4.93%)	1 / 6 (16.67%)	3 / 21 (14.29%)
occurrences (all)	26	1	3
Hyperglycaemia			
subjects affected / exposed	42 / 406 (10.34%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	80	0	2
Hypercholesterolaemia			
subjects affected / exposed	27 / 406 (6.65%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	39	0	0
Dehydration			
subjects affected / exposed	22 / 406 (5.42%)	0 / 6 (0.00%)	0 / 21 (0.00%)
occurrences (all)	29	0	0
Decreased appetite			
subjects affected / exposed	184 / 406 (45.32%)	3 / 6 (50.00%)	4 / 21 (19.05%)
occurrences (all)	253	5	5
Hypercalcaemia			
subjects affected / exposed	21 / 406 (5.17%)	0 / 6 (0.00%)	1 / 21 (4.76%)
occurrences (all)	24	0	1
Hypophosphataemia			
subjects affected / exposed	20 / 406 (4.93%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	29	1	2
Hyponatraemia			
subjects affected / exposed	38 / 406 (9.36%)	1 / 6 (16.67%)	1 / 21 (4.76%)
occurrences (all)	49	1	1
Hypomagnesaemia			
subjects affected / exposed	80 / 406 (19.70%)	3 / 6 (50.00%)	2 / 21 (9.52%)
occurrences (all)	148	3	3
Hypokalaemia			
subjects affected / exposed	60 / 406 (14.78%)	1 / 6 (16.67%)	2 / 21 (9.52%)
occurrences (all)	72	1	4
Hypoalbuminaemia			

subjects affected / exposed	40 / 406 (9.85%)	0 / 6 (0.00%)	2 / 21 (9.52%)
occurrences (all)	56	0	5

Non-serious adverse events	First Course: TPC Doxorubicin or Paclitaxel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	379 / 388 (97.68%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 388 (5.15%)		
occurrences (all)	28		
Hot flush			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	8		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	93 / 388 (23.97%)		
occurrences (all)	124		
Pyrexia			
subjects affected / exposed	26 / 388 (6.70%)		
occurrences (all)	29		
Oedema peripheral			
subjects affected / exposed	36 / 388 (9.28%)		
occurrences (all)	40		
Mucosal inflammation			
subjects affected / exposed	38 / 388 (9.79%)		
occurrences (all)	47		
Malaise			
subjects affected / exposed	19 / 388 (4.90%)		
occurrences (all)	29		
Fatigue			
subjects affected / exposed	107 / 388 (27.58%)		
occurrences (all)	146		
Chest pain			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	8		
Reproductive system and breast			

disorders			
Breast pain			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	12 / 388 (3.09%)		
occurrences (all)	14		
Vulvovaginal pruritus			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	4 / 388 (1.03%)		
occurrences (all)	4		
Productive cough			
subjects affected / exposed	4 / 388 (1.03%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	9 / 388 (2.32%)		
occurrences (all)	11		
Epistaxis			
subjects affected / exposed	11 / 388 (2.84%)		
occurrences (all)	13		
Dyspnoea exertional			
subjects affected / exposed	4 / 388 (1.03%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	43 / 388 (11.08%)		
occurrences (all)	45		
Dysphonia			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	51 / 388 (13.14%)		
occurrences (all)	55		
Psychiatric disorders			

Anxiety			
subjects affected / exposed	10 / 388 (2.58%)		
occurrences (all)	11		
Insomnia			
subjects affected / exposed	20 / 388 (5.15%)		
occurrences (all)	21		
Initial insomnia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	15 / 388 (3.87%)		
occurrences (all)	19		
Blood bilirubin increased			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	10		
Blood calcium decreased			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences (all)	2		
Blood chloride decreased			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences (all)	1		
Blood cholesterol increased			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	9		
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 388 (4.12%)		
occurrences (all)	17		
Amylase increased			
subjects affected / exposed	5 / 388 (1.29%)		
occurrences (all)	7		
Alanine aminotransferase increased			

subjects affected / exposed	22 / 388 (5.67%)		
occurrences (all)	28		
Blood creatinine increased			
subjects affected / exposed	10 / 388 (2.58%)		
occurrences (all)	10		
Blood lactate dehydrogenase increased			
subjects affected / exposed	12 / 388 (3.09%)		
occurrences (all)	13		
Blood magnesium decreased			
subjects affected / exposed	6 / 388 (1.55%)		
occurrences (all)	7		
Blood phosphorus decreased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Blood sodium decreased			
subjects affected / exposed	4 / 388 (1.03%)		
occurrences (all)	4		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences (all)	2		
Blood urea increased			
subjects affected / exposed	4 / 388 (1.03%)		
occurrences (all)	6		
International normalised ratio increased			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	8 / 388 (2.06%)		
occurrences (all)	9		
Lymphocyte count decreased			
subjects affected / exposed	24 / 388 (6.19%)		
occurrences (all)	32		
Neutrophil count decreased			

subjects affected / exposed	95 / 388 (24.48%)		
occurrences (all)	220		
Platelet count decreased			
subjects affected / exposed	23 / 388 (5.93%)		
occurrences (all)	28		
Weight decreased			
subjects affected / exposed	23 / 388 (5.93%)		
occurrences (all)	24		
White blood cell count decreased			
subjects affected / exposed	63 / 388 (16.24%)		
occurrences (all)	147		
White blood cell count increased			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences (all)	3		
Nervous system disorders			
Taste disorder			
subjects affected / exposed	5 / 388 (1.29%)		
occurrences (all)	6		
Neuropathy peripheral			
subjects affected / exposed	23 / 388 (5.93%)		
occurrences (all)	24		
Headache			
subjects affected / exposed	35 / 388 (9.02%)		
occurrences (all)	36		
Dysgeusia			
subjects affected / exposed	29 / 388 (7.47%)		
occurrences (all)	36		
Dizziness			
subjects affected / exposed	22 / 388 (5.67%)		
occurrences (all)	29		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	181 / 388 (46.65%)		
occurrences (all)	240		
Lymphopenia			

subjects affected / exposed	30 / 388 (7.73%)		
occurrences (all)	45		
Leukopenia			
subjects affected / exposed	50 / 388 (12.89%)		
occurrences (all)	89		
Thrombocytopenia			
subjects affected / exposed	26 / 388 (6.70%)		
occurrences (all)	31		
Neutropenia			
subjects affected / exposed	125 / 388 (32.22%)		
occurrences (all)	213		
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye pruritus			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences (all)	1		
Diplopia			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	52 / 388 (13.40%)		
occurrences (all)	58		
Abdominal discomfort			
subjects affected / exposed	5 / 388 (1.29%)		
occurrences (all)	5		
Abdominal pain upper			
subjects affected / exposed	28 / 388 (7.22%)		
occurrences (all)	34		
Nausea			
subjects affected / exposed	179 / 388 (46.13%)		
occurrences (all)	302		
Intestinal obstruction			

subjects affected / exposed	3 / 388 (0.77%)		
occurrences (all)	3		
Haemorrhoids			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	9		
Gastrooesophageal reflux disease			
subjects affected / exposed	8 / 388 (2.06%)		
occurrences (all)	8		
Odynophagia			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences (all)	3		
Dyspepsia			
subjects affected / exposed	20 / 388 (5.15%)		
occurrences (all)	20		
Dry mouth			
subjects affected / exposed	12 / 388 (3.09%)		
occurrences (all)	16		
Diarrhoea			
subjects affected / exposed	76 / 388 (19.59%)		
occurrences (all)	107		
Constipation			
subjects affected / exposed	95 / 388 (24.48%)		
occurrences (all)	119		
Gastritis			
subjects affected / exposed	2 / 388 (0.52%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	80 / 388 (20.62%)		
occurrences (all)	122		
Stomatitis			
subjects affected / exposed	46 / 388 (11.86%)		
occurrences (all)	58		
Oral pain			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			

Pemphigoid			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	12 / 388 (3.09%)		
occurrences (all)	12		
Rash			
subjects affected / exposed	13 / 388 (3.35%)		
occurrences (all)	13		
Rash pruritic			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	11 / 388 (2.84%)		
occurrences (all)	11		
Dermatitis			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	120 / 388 (30.93%)		
occurrences (all)	120		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	13 / 388 (3.35%)		
occurrences (all)	15		
Leukocyturia			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	11 / 388 (2.84%)		
occurrences (all)	13		
Endocrine disorders			

Hypothyroidism subjects affected / exposed occurrences (all)	3 / 388 (0.77%) 3		
Hyperthyroidism subjects affected / exposed occurrences (all)	4 / 388 (1.03%) 4		
Musculoskeletal and connective tissue disorders			
Myalgia subjects affected / exposed occurrences (all)	20 / 388 (5.15%) 25		
Muscle spasms subjects affected / exposed occurrences (all)	8 / 388 (2.06%) 9		
Bone pain subjects affected / exposed occurrences (all)	10 / 388 (2.58%) 10		
Back pain subjects affected / exposed occurrences (all)	30 / 388 (7.73%) 37		
Arthralgia subjects affected / exposed occurrences (all)	31 / 388 (7.99%) 33		
Pain in extremity subjects affected / exposed occurrences (all)	22 / 388 (5.67%) 26		
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	17 / 388 (4.38%) 20		
Tinea infection subjects affected / exposed occurrences (all)	2 / 388 (0.52%) 2		
Respiratory tract infection subjects affected / exposed occurrences (all)	4 / 388 (1.03%) 5		
Oral herpes			

subjects affected / exposed	5 / 388 (1.29%)		
occurrences (all)	7		
COVID-19			
subjects affected / exposed	0 / 388 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	8 / 388 (2.06%)		
occurrences (all)	9		
Fungal foot infection			
subjects affected / exposed	1 / 388 (0.26%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	8 / 388 (2.06%)		
occurrences (all)	8		
Cellulitis			
subjects affected / exposed	5 / 388 (1.29%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	24 / 388 (6.19%)		
occurrences (all)	29		
Urinary tract infection			
subjects affected / exposed	39 / 388 (10.05%)		
occurrences (all)	49		
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	12 / 388 (3.09%)		
occurrences (all)	14		
Hyperkalaemia			
subjects affected / exposed	4 / 388 (1.03%)		
occurrences (all)	4		
Hyperglycaemia			
subjects affected / exposed	19 / 388 (4.90%)		
occurrences (all)	24		
Hypercholesterolaemia			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	11		

Dehydration			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	7		
Decreased appetite			
subjects affected / exposed	83 / 388 (21.39%)		
occurrences (all)	99		
Hypercalcaemia			
subjects affected / exposed	3 / 388 (0.77%)		
occurrences (all)	3		
Hypophosphataemia			
subjects affected / exposed	7 / 388 (1.80%)		
occurrences (all)	10		
Hyponatraemia			
subjects affected / exposed	16 / 388 (4.12%)		
occurrences (all)	16		
Hypomagnesaemia			
subjects affected / exposed	27 / 388 (6.96%)		
occurrences (all)	30		
Hypokalaemia			
subjects affected / exposed	26 / 388 (6.70%)		
occurrences (all)	35		
Hypoalbuminaemia			
subjects affected / exposed	18 / 388 (4.64%)		
occurrences (all)	20		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 March 2018	The major changes of amendment (AM) 1 were to address Germany country-specific request for viral serology testing and pregnancy testing.
06 June 2018	The major changes of amendment AM 2 were to address United Kingdom (UK) country-specific requests for viral serology testing and contraception use.
31 August 2018	The major changes of amendment AM 3 were to provide clarity with respect to the number of prior lines of treatment in order to be eligible for the study.
01 October 2018	The major changes of amendment AM 4 were to address Germany country-specific requests for serology and to provide clarity with respect to the number of prior lines of treatment in order to be eligible for the study.
02 October 2018	The major changes of amendment AM 5 were to address UK country-specific requests for serology and to provide clarity with respect to the number of prior lines of treatment in order to be eligible for the study
18 February 2020	The major changes of amendment AM 6 were to revise statistical analysis plan to add an interim efficacy analysis to evaluate the superiority of PFS and OS
12 June 2020	The major changes of amendment AM 7 were to revise statistical analysis plan to revise timing interim efficacy analysis post health authority communications
15 June 2021	The major changes of amendment AM 8 were to allow crossover from TPC to the lenvatinib plus pembrolizumab arm at time of progression and to remove interim analysis 2 since primary objectives already met, including the final analysis of PFS.
22 November 2022	The major changes of amendment AM 9 were to add extension study and to remove the collection of further Patient reported outcome (PRO) data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported