



## Clinical trial results:

**A multicentre randomised phase III trial comparing atezolizumab plus bevacizumab and standard chemotherapy versus bevacizumab and standard chemotherapy as first-line treatment for advanced malignant pleural mesothelioma**

### Summary

EudraCT number	2018-002180-25
Trial protocol	BE GB FR IT
Global end of trial date	18 November 2024

### Results information

Result version number	v1 (current)
This version publication date	18 March 2026
First version publication date	18 March 2026

### Trial information

#### Trial identification

Sponsor protocol code	ETOP 13-18 BEAT-meso
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03762018
WHO universal trial number (UTN)	-
Other trial identifiers	Roche Number: MO40388

Notes:

### Sponsors

Sponsor organisation name	ETOP IBCSG Partners Foundation
Sponsor organisation address	Effingerstrasse 33, Bern, Switzerland, 3008
Public contact	ETOP IBCSG Partners Coordinating Center, ETOP IBCSG Partners Foundation, +41 315119400, etop-regulatory@etop.ibcsg.org
Scientific contact	ETOP IBCSG Partners Coordinating Center, ETOP IBCSG Partners Foundation, +41 315119400, etop-regulatory@etop.ibcsg.org

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	25 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2023
Global end of trial reached?	Yes
Global end of trial date	18 November 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The objective of this trial is to assess the effect of atezolizumab in terms of PFS and OS when added to standard of care (carboplatin/pemetrexed/bevacizumab), as first-line treatment of advanced MPM.

Protection of trial subjects:

Participating institutions' ethics committees or Institutional Review Boards approved the trial according to local laws and regulations. All patients gave written informed consent, and the trial was performed in compliance with the Helsinki Declaration. The Data Safety and Monitoring Board reviewed the data from this research throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2019
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	Switzerland: 66
Country: Number of subjects enrolled	Spain: 84
Country: Number of subjects enrolled	United Kingdom: 139
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Italy: 68
Worldwide total number of subjects	400
EEA total number of subjects	195

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)	102
From 65 to 84 years	292
85 years and over	6

## Subject disposition

### Recruitment

Recruitment details:

Overall, 400 patients were randomized from April 30, 2019 to March 07, 2022 (randomization date of the last patient). Randomized patients come from 38 centers in 6 European countries (10 in United Kingdom, 9 in Switzerland, 7 in Spain, 6 in Italy, 4 in France, 2 in Belgium).

### Pre-assignment

Screening details:

46 patients were not randomized in the trial, indicated as screening failures.

### 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
<b>Arm title</b>	ABC Arm

Arm description:

4-6 cycles chemotherapy: Carboplatin AUC 5 + pemetrexed 500 mg/m<sup>2</sup>, D1Q3W plus  
Bevacizumab 15mg/kg D1Q3W until PD, refusal or unacceptable toxicity plus  
Atezolizumab 1200 mg D1Q3W until PD, refusal or unacceptable toxicity

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

Dosage and administration details:

1200 mg D1Q3W until PD, refusal or unacceptable toxicity

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15mg/kg D1Q3W until PD, refusal or unacceptable toxicity

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4-6 cycles chemotherapy: Carboplatin AUC 5, D1Q3W

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4-6 cycles chemotherapy: pemetrexed 500 mg/m<sup>2</sup>, D1Q3W

<b>Arm title</b>	BC Arm
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Arm description:

4-6 cycles chemotherapy: Carboplatin AUC 5 + pemetrexed 500 mg/m<sup>2</sup>, D1Q3W plus

Bevacizumab 15mg/kg D1Q3W until PD, refusal or unacceptable toxicity

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

Dosage and administration details:

15mg/kg D1Q3W until PD, refusal or unacceptable toxicity

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4-6 cycles chemotherapy: Carboplatin AUC 5, D1Q3W

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4-6 cycles chemotherapy: pemetrexed 500 mg/m<sup>2</sup>, D1Q3W

<b>Number of subjects in period 1</b>	ABC Arm	BC Arm
Started	200	200
Completed	51	48
Not completed	149	152
Death	145	150
Withdrawal/Lost to follow-up	4	2

## Baseline characteristics

### Reporting groups

Reporting group title	ABC Arm
Reporting group description: 4-6 cycles chemotherapy: Carboplatin AUC 5 + pemetrexed 500 mg/m2, D1Q3W plus Bevacizumab 15mg/kg D1Q3W until PD, refusal or unacceptable toxicity plus Atezolizumab 1200 mg D1Q3W until PD, refusal or unacceptable toxicity	
Reporting group title	BC Arm
Reporting group description: 4-6 cycles chemotherapy: Carboplatin AUC 5 + pemetrexed 500 mg/m2, D1Q3W plus Bevacizumab 15mg/kg D1Q3W until PD, refusal or unacceptable toxicity	

Reporting group values	ABC Arm	BC Arm	Total
Number of subjects	200	200	400
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	70.7	70.1	
full range (min-max)	42.3 to 87.6	47.7 to 88.2	-
Gender categorical Units: Subjects			
Female	40	44	84
Male	160	156	316
Race/Ethnicity, Customized Units: Subjects			
White	199	200	399
Black	1	0	1
Smoking status			
Current smoker: Still smokes cigarettes, Former smoker: Smoked at least 100 cigarettes in the past during the whole life, Never smoker: Smoked 0-99 cigarettes during the whole life.			
Units: Subjects			
Current smoker	15	11	26
Former smoker	99	99	198
Never smoked	86	90	176
ECOG Performance Status			
0: Fully active, able to carry on all pre-disease performance without restriction; 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.			

g., light house work, office work.			
Units: Subjects			
Status 0	80	61	141
Status 1	119	139	258
Unknown/Missing	1	0	1
Stage			
Stage is based on the 8th TNM classification for Malignant Pleural Mesothelioma (American Joint Committee on Cancer).			
Units: Subjects			
IV	43	41	84
Other	157	159	316
Histology			
Units: Subjects			
Epitheloid	157	154	311
Non pure epitheloid	43	46	89
Asbestos exposure			
Units: Subjects			
Yes	84	89	173
Possible	51	58	109
No	48	33	81
Unknown/Missing	17	20	37
PD-L1 TPS%			
Units: Subjects			
<1	117	98	215
1-49	56	66	122
≥50	21	26	47
Unknown/Missing	6	10	16
EORTC prognostic score			
EORTC PROGNOSTIC SCORE: Curran et al. Journal of Clinical Oncology. 1998 Jan; Vol16:145-152			
Units: Subjects			
Good prognosis	146	134	280
Poor prognosis	54	66	120
Mesothelioma risk score (MRS)			
Mesothelioma risk score (MRS): Banna et al. Lung Cancer. 2022 Jul; 169:77-83 The risk factors are baseline systemic immune-inflammatory index (good: < 1,250 vs poor: ≥ 1,250) and baseline haemoglobin (good: ≥ LLN vs poor: < LLN) (LLN = 135 for males, LLN = 120 for females))			
Units: Subjects			
0-Favorable	72	64	136
1-Intermediate	66	63	129
2-Poor	62	73	135
Medical history			
Units: Subjects			
Yes	189	187	376
No	11	13	24

## End points

### End points reporting groups

Reporting group title	ABC Arm
Reporting group description: 4-6 cycles chemotherapy: Carboplatin AUC 5 + pemetrexed 500 mg/m2, D1Q3W plus Bevacizumab 15mg/kg D1Q3W until PD, refusal or unacceptable toxicity plus Atezolizumab 1200 mg D1Q3W until PD, refusal or unacceptable toxicity	
Reporting group title	BC Arm
Reporting group description: 4-6 cycles chemotherapy: Carboplatin AUC 5 + pemetrexed 500 mg/m2, D1Q3W plus Bevacizumab 15mg/kg D1Q3W until PD, refusal or unacceptable toxicity	

### Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description: Overall survival is defined as the time from the date of randomisation until death from any cause. Data for patients who are not reported as having died at the date of analysis will be censored at the date when they were last known to be alive. Data for patients without post-baseline information will be censored at the date of randomization (plus 1 day).	
End point type	Primary
End point timeframe: Evaluated up to approximately 58 months from the randomisation of the first patient.	

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200 <sup>[1]</sup>	200 <sup>[2]</sup>		
Units: month				
median (confidence interval 95%)	20.5 (17.5 to 23.3)	18.1 (15.7 to 20.9)		

Notes:

[1] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

[2] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

### Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: The study was designed to test the hypothesis that addition of Atezolizumab to Bevacizumab and chemotherapy leads to an increase in median OS from 17 months with Bevacizumab and chemotherapy alone to 24 months. According to the study design, this corresponds to a HR of 0.708. Using the log-rank test stratified by the randomization stratification factors (histological subtype and stage), 284 deaths were required to achieve the trial goal with 82.1% power at a 1-sided significance level of 2.5%.	
Comparison groups	BC Arm v ABC Arm



Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14 <sup>[3]</sup>
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.06

Notes:

[3] - 1-sided significance level of 2.5%.

### Secondary: Progression-free Survival (PFS) according to the mRECIST v1.1

End point title	Progression-free Survival (PFS) according to the mRECIST v1.1
End point description:	
PFS is defined as the time from the date of randomisation until documented progression (according to the mRECIST v1.1) or death, if progression is not documented. Censoring (for participants without a PFS/death event) will occur at the date of last tumour assessment. Patients without a post-baseline tumour assessment will be censored at the date of randomization (plus 1 day).	
End point type	Secondary
End point timeframe:	
Evaluated up to approximately 58 months from the randomisation of the first patient.	

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200 <sup>[4]</sup>	200 <sup>[5]</sup>		
Units: Month				
median (confidence interval 95%)	9.2 (8.1 to 10.9)	7.6 (6.9 to 8.3)		

Notes:

[4] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

[5] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
Objective Response Rate (ORR) is defined as the percentage of patients that achieve a best overall response [complete response (CR) or partial response (PR)] evaluated according to the mRECIST v1.1 across all post-randomization time-points until the end of protocol treatment. Confirmation of response will not be required.	
End point type	Secondary
End point timeframe:	
Evaluated up to approximately 58 months from the randomisation of the first patient.	

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200 <sup>[6]</sup>	200 <sup>[7]</sup>		
Units: Participant	110	98		

Notes:

[6] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

[7] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Disease Control (DC) at 24 weeks

End point title	Disease Control (DC) at 24 weeks
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End point description:

Disease Control (DC) is defined as complete or partial response, or disease stabilisation at 24 weeks (+/- 10 days). Patients with no available scan at this time period, but with scan performed before 24 weeks - 10 days and scan performed after 24 weeks + 10 days showing disease control, will be considered as disease control.

End point type	Secondary
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End point timeframe:

Evaluated up to approximately 58 months from the randomisation of the first patient.

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200 <sup>[8]</sup>	200 <sup>[9]</sup>		
Units: Participant	134	115		

Notes:

[8] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

[9] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Treatment Failure (TTF)

End point title	Time to Treatment Failure (TTF)
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End point description:

Time to Treatment Failure (TTF) is defined as the time from the date of randomisation to discontinuation of protocol treatment for any reason (including progression of disease, death, discontinuation of at least one of the drugs consisting the treatment combination due to any reason, such as toxicity or refusal). Censoring will occur at the last follow-up date.

End point type	Secondary
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End point timeframe:

Evaluated up to approximately 58 months from the randomisation of the first patient.

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200 <sup>[10]</sup>	200 <sup>[11]</sup>		
Units: month				
median (confidence interval 95%)	6.5 (5.6 to 7.4)	6.5 (5.7 to 7.0)		

Notes:

[10] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

[11] - Efficacy population (Intention-To-Treat cohort of all randomised patients)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
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End point description:

Duration of Response (DoR) is defined as the interval from the date of first documentation of objective response (complete response or partial response, according to the mRECIST v1.1) to the date of first documented progression/relapse or death.

End point type	Secondary
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End point timeframe:

Evaluated up to approximately 58 months from the randomisation of the first patient.

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110 <sup>[12]</sup>	98 <sup>[13]</sup>		
Units: Month				
median (confidence interval 95%)	8.2 (6.8 to 9.7)	5.6 (4.8 to 7.0)		

Notes:

[12] - Patients with objective response

[13] - Patients with objective response

## Statistical analyses

No statistical analyses for this end point

## Secondary: Quality of Life (QoL)

End point title	Quality of Life (QoL)
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End point description:

QoL will be assessed by the Lung Cancer Symptom Scale-Mesothelioma (LCSS-Meso) an 8-item questionnaire including five symptoms (i.e., appetite loss, fatigue, cough, dyspnoea, and pain) and three items addressing symptomatic distress, normal activity, and global QoL. The primary QoL endpoint will be the change in the LCSS total score (average of all 8 items) from baseline to 12 weeks after treatment start.

End point type	Secondary
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End point timeframe:

Evaluated up to approximately 58 months from the randomisation of the first patient.

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157 <sup>[14]</sup>	155 <sup>[15]</sup>		
Units: Change in the LCSS average total score				
median (confidence interval 95%)	0.4 (-2.3 to 3.0)	2.1 (-0.4 to 4.7)		

Notes:

[14] - rando pts who had baseline assessment & at least 1 on-treatment post-baseline score for any LCSS-Meso item

[15] - rando pts who had baseline assessment & at least 1 on-treatment post-baseline score for any LCSS-Meso item

### Statistical analyses

No statistical analyses for this end point

### Secondary: Adverse Events

End point title	Adverse Events
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End point description:

Adverse events, according to CTCAE v5.0, will be recorded from date of signature of informed consent until 90 days after the last dose of protocol treatment.

#### Analysis Population Description

Safety population (all patients who received at least 1 dose of trial treatment). There is one patient assigned in the BC arm who actually received ABC treatment. For the safety analysis the patient is evaluated according to the treatment he/she received (ABC treatment), irrespective of the allocated treatment at randomization.

End point type	Secondary
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End point timeframe:

Evaluated up to approximately 58 months from the randomisation of the first patient.

End point values	ABC Arm	BC Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	199		
Units: Participant	197	197		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From date of signature of informed consent until 90 days after the last dose of protocol treatment

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	5.0
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### Reporting groups

Reporting group title	ABC Arm
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Reporting group description:

There is one patient assigned in the BC arm who actually received ABC treatment.

For the safety analysis the patient is evaluated according to the treatment he/she received (ABC treatment), irrespective of the allocated treatment at randomization

Reporting group title	BC Arm
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Reporting group description: -

Serious adverse events	ABC Arm	BC Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	94 / 199 (47.24%)	64 / 199 (32.16%)	
number of deaths (all causes)	145	150	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukemia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate adenocarcinoma			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell neuroendocrine carcinoma			

subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary bladder nodule (left trigone region)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial thromboembolism			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematoma			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischemia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial thrombophlebitis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			

subjects affected / exposed	5 / 199 (2.51%)	5 / 199 (2.51%)	
occurrences causally related to treatment / all	4 / 5	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Elective surgery popliteal aneurysm			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Fever			
subjects affected / exposed	8 / 199 (4.02%)	4 / 199 (2.01%)	
occurrences causally related to treatment / all	6 / 8	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flu like symptoms			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General clinical conditions worsening			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General status alteration			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalized edema			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar spine joint range of motion decreased			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	1 / 199 (0.50%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune disorder			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchopulmonary hemorrhage			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease (COPD)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea			



subjects affected / exposed	6 / 199 (3.02%)	4 / 199 (2.01%)	
occurrences causally related to treatment / all	3 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Organized pneumonia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuric pain			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	3 / 199 (1.51%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Asystole			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain - cardiac			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart failure			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	3 / 199 (1.51%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

Supraventricular tachycardia subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cognitive disturbance subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial hemorrhage subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Neuralgia subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Blood and lymphatic system disorders</b>			
<b>Anemia</b>			
subjects affected / exposed	5 / 199 (2.51%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	4 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Febrile neutropenia</b>			
subjects affected / exposed	6 / 199 (3.02%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	6 / 6	2 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
<b>Immune thrombocytopenic purpura</b>			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pancytopenia</b>			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal disorders</b>			
<b>Abdominal pain</b>			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Anal fistula</b>			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Colitis</b>			
subjects affected / exposed	1 / 199 (0.50%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Colonic obstruction</b>			

subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic perforation			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Constipation			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric hemorrhage			
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal hemorrhage			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal perforation			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhlitis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Bullous dermatitis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulceration			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematuria			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	3 / 199 (1.51%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal biopsy			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal toxicity			

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Infections and infestations			
Bacteremia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	



COVID-19 infection			
subjects affected / exposed	7 / 199 (3.52%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	1 / 7	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Device related infection			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungemia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection (unknown source)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	9 / 199 (4.52%)	12 / 199 (6.03%)	
occurrences causally related to treatment / all	2 / 9	5 / 12	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pleural infection			
subjects affected / exposed	3 / 199 (1.51%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Port-a-cath infection			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	8 / 199 (4.02%)	6 / 199 (3.02%)	
occurrences causally related to treatment / all	8 / 8	4 / 6	
deaths causally related to treatment / all	3 / 3	0 / 2	
Skin infection			

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory infection			
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcemia			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycemia			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycemia			

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesemia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	ABC Arm	BC Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	197 / 199 (98.99%)	197 / 199 (98.99%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cyst buttock (right)			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Nasal polyp			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Tumor pain			
subjects affected / exposed	2 / 199 (1.01%)	8 / 199 (4.02%)	
occurrences (all)	2	8	
Vascular disorders			
Arterial thromboembolism			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Hematoma			

subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Hot flashes			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences (all)	2	1	
Hypertension			
subjects affected / exposed	72 / 199 (36.18%)	62 / 199 (31.16%)	
occurrences (all)	72	62	
Hypotension			
subjects affected / exposed	5 / 199 (2.51%)	3 / 199 (1.51%)	
occurrences (all)	5	3	
Intracranial aneurysm			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Leg capillaritis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Lymphedema			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Phlebitis			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences (all)	2	1	
Pulmonary arteria infiltration			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Superficial thrombophlebitis			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences (all)	2	1	
Sylvic bifurcation aneurysm (right)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Thromboembolic event			
subjects affected / exposed	16 / 199 (8.04%)	8 / 199 (4.02%)	
occurrences (all)	16	8	
Surgical and medical procedures			

Cataract surgery			
subjects affected / exposed	0 / 199 (0.00%)	3 / 199 (1.51%)	
occurrences (all)	0	3	
Central venous access device surgery			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Dental surgery			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Drain removal			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Electrophysiology			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Exophytic lingual lesion extraction			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Eyelid intervention (left)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Pleurectomy (left radical decortication)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Port-a-cath blockage			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Tooth extraction			
subjects affected / exposed	4 / 199 (2.01%)	1 / 199 (0.50%)	
occurrences (all)	4	1	
Total hip replacement (left)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Asthenia		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Chills		
subjects affected / exposed	2 / 199 (1.01%)	3 / 199 (1.51%)
occurrences (all)	2	3
Cold syndrome		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Dysphonia		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Edema face		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Edema limbs		
subjects affected / exposed	21 / 199 (10.55%)	15 / 199 (7.54%)
occurrences (all)	21	15
Edema trunk		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Facial pain		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Fatigue		
subjects affected / exposed	113 / 199 (56.78%)	110 / 199 (55.28%)
occurrences (all)	113	110
Fever		
subjects affected / exposed	35 / 199 (17.59%)	13 / 199 (6.53%)
occurrences (all)	35	13
Flu like symptoms		
subjects affected / exposed	9 / 199 (4.52%)	8 / 199 (4.02%)
occurrences (all)	9	8
Gait disturbance		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1

General clinical conditions worsening		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
General status alteration		
subjects affected / exposed	3 / 199 (1.51%)	0 / 199 (0.00%)
occurrences (all)	3	0
General weakness		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Generalized edema		
subjects affected / exposed	0 / 199 (0.00%)	4 / 199 (2.01%)
occurrences (all)	0	4
Gout		
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)
occurrences (all)	2	1
Hypersalivation		
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)
occurrences (all)	0	2
Infusion site extravasation		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Injection site reaction		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Localized edema		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Malaise		
subjects affected / exposed	4 / 199 (2.01%)	4 / 199 (2.01%)
occurrences (all)	4	4
Metallic taste		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Non-cardiac chest pain		
subjects affected / exposed	31 / 199 (15.58%)	36 / 199 (18.09%)
occurrences (all)	31	36

Pain			
subjects affected / exposed	14 / 199 (7.04%)	21 / 199 (10.55%)	
occurrences (all)	14	21	
Penis red lesions			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Proximal myopathy			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Tingling knee			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Cholestasis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	5 / 199 (2.51%)	2 / 199 (1.01%)	
occurrences (all)	5	2	
Polymyalgia rheumatica-like syndrome			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
Reduced mobility			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Split lip			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Genital edema			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	



Gynecomastia			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Pelvic pain			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Penile pain			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Prostate hypertrophy			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Testicular swelling			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Allergic rhinitis			
subjects affected / exposed	6 / 199 (3.02%)	3 / 199 (1.51%)	
occurrences (all)	6	3	
Bloody sputum			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Bronchial obstruction			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Bronchopulmonary hemorrhage			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Bronchospasm			
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)	
occurrences (all)	0	2	
Cough			
subjects affected / exposed	33 / 199 (16.58%)	32 / 199 (16.08%)	
occurrences (all)	33	32	
Dry nasal			

subjects affected / exposed	1 / 199 (0.50%)	2 / 199 (1.01%)
occurrences (all)	1	2
Dry nose		
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)
occurrences (all)	0	2
Dyspnea		
subjects affected / exposed	38 / 199 (19.10%)	47 / 199 (23.62%)
occurrences (all)	38	47
Epistaxis		
subjects affected / exposed	56 / 199 (28.14%)	56 / 199 (28.14%)
occurrences (all)	56	56
Hemoptysis		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Hiccups		
subjects affected / exposed	2 / 199 (1.01%)	5 / 199 (2.51%)
occurrences (all)	2	5
Hoarseness		
subjects affected / exposed	11 / 199 (5.53%)	9 / 199 (4.52%)
occurrences (all)	11	9
Hypoxia		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Interstitial lung infiltrates		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Laryngeal inflammation		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Laryngeal mucositis		
subjects affected / exposed	1 / 199 (0.50%)	2 / 199 (1.01%)
occurrences (all)	1	2
Nasal congestion		
subjects affected / exposed	2 / 199 (1.01%)	5 / 199 (2.51%)
occurrences (all)	2	5
Nocturnal mucus		

subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Oropharyngeal pain		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Pharyngeal mucositis		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Pharyngolaryngeal pain		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Phlegm		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Pleural drainage insertion site pain		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Pleural effusion		
subjects affected / exposed	3 / 199 (1.51%)	2 / 199 (1.01%)
occurrences (all)	3	2
Pleuritic pain		
subjects affected / exposed	5 / 199 (2.51%)	10 / 199 (5.03%)
occurrences (all)	5	10
Pneumonitis		
subjects affected / exposed	1 / 199 (0.50%)	3 / 199 (1.51%)
occurrences (all)	1	3
Pneumothorax		
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)
occurrences (all)	2	1
Postnasal drip		
subjects affected / exposed	3 / 199 (1.51%)	0 / 199 (0.00%)
occurrences (all)	3	0
Productive cough		
subjects affected / exposed	4 / 199 (2.01%)	5 / 199 (2.51%)
occurrences (all)	4	5
Pulmonary edema		

subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	1 / 199 (0.50%) 1	
Rhinorrhea			
subjects affected / exposed occurrences (all)	11 / 199 (5.53%) 11	17 / 199 (8.54%) 17	
Sinus disorder			
subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	2 / 199 (1.01%) 2	
Sore throat			
subjects affected / exposed occurrences (all)	5 / 199 (2.51%) 5	3 / 199 (1.51%) 3	
Voice alteration			
subjects affected / exposed occurrences (all)	6 / 199 (3.02%) 6	8 / 199 (4.02%) 8	
Wheezing			
subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	1 / 199 (0.50%) 1	
Psychiatric disorders			
Agitation			
subjects affected / exposed occurrences (all)	4 / 199 (2.01%) 4	2 / 199 (1.01%) 2	
Anxiety			
subjects affected / exposed occurrences (all)	9 / 199 (4.52%) 9	9 / 199 (4.52%) 9	
Conduct disorder			
subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Confusion			
subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	2 / 199 (1.01%) 2	
Delirium			
subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Depression			
subjects affected / exposed occurrences (all)	6 / 199 (3.02%) 6	11 / 199 (5.53%) 11	

Insomnia			
subjects affected / exposed	19 / 199 (9.55%)	16 / 199 (8.04%)	
occurrences (all)	19	16	
Irritability			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Libido increased			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Mood change			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Nightmares			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	26 / 199 (13.07%)	25 / 199 (12.56%)	
occurrences (all)	26	25	
Alkaline phosphatase increased			
subjects affected / exposed	6 / 199 (3.02%)	6 / 199 (3.02%)	
occurrences (all)	6	6	
Aspartate aminotransferase increased			
subjects affected / exposed	24 / 199 (12.06%)	21 / 199 (10.55%)	
occurrences (all)	24	21	
Blood bilirubin increased			
subjects affected / exposed	3 / 199 (1.51%)	1 / 199 (0.50%)	
occurrences (all)	3	1	
Blood corticotrophin decreased			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 199 (2.51%)	2 / 199 (1.01%)	
occurrences (all)	5	2	
C-reactive protein increased			

subjects affected / exposed	3 / 199 (1.51%)	2 / 199 (1.01%)
occurrences (all)	3	2
CPK increased		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Cardiac troponin T increased		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Cholesterol high		
subjects affected / exposed	5 / 199 (2.51%)	1 / 199 (0.50%)
occurrences (all)	5	1
Creatinine decreased		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Creatinine increased		
subjects affected / exposed	39 / 199 (19.60%)	24 / 199 (12.06%)
occurrences (all)	39	24
Electrocardiogram QT corrected interval prolonged		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
GGT increased		
subjects affected / exposed	14 / 199 (7.04%)	15 / 199 (7.54%)
occurrences (all)	14	15
Hemoglobin increased		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
INR increased		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Iron deficiency		
subjects affected / exposed	1 / 199 (0.50%)	2 / 199 (1.01%)
occurrences (all)	1	2
Lipase increased		
subjects affected / exposed	7 / 199 (3.52%)	6 / 199 (3.02%)
occurrences (all)	7	6

Lymphocyte count decreased subjects affected / exposed occurrences (all)	4 / 199 (2.01%) 4	4 / 199 (2.01%) 4
Lymphocyte count increased subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	63 / 199 (31.66%) 63	56 / 199 (28.14%) 56
Neutrophil count increased subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1
Pancreatic amylase subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	39 / 199 (19.60%) 39	24 / 199 (12.06%) 24
Platelet count increased subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Prostate-specific antigen (PSA) increased subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Serum amylase increased subjects affected / exposed occurrences (all)	16 / 199 (8.04%) 16	13 / 199 (6.53%) 13
Serum urea increased subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	5 / 199 (2.51%) 5	1 / 199 (0.50%) 1
Urea increased		

subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Weight gain subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	1 / 199 (0.50%) 1	
Weight loss subjects affected / exposed occurrences (all)	15 / 199 (7.54%) 15	11 / 199 (5.53%) 11	
White blood cell decreased subjects affected / exposed occurrences (all)	14 / 199 (7.04%) 14	9 / 199 (4.52%) 9	
Hypoglycemia subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	2 / 199 (1.01%) 2	
Injury, poisoning and procedural complications			
Bruising subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	3 / 199 (1.51%) 3	
Burn subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Fall subjects affected / exposed occurrences (all)	5 / 199 (2.51%) 5	1 / 199 (0.50%) 1	
Fracture subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	2 / 199 (1.01%) 2	
Infusion related reaction subjects affected / exposed occurrences (all)	15 / 199 (7.54%) 15	3 / 199 (1.51%) 3	
Port dehiscence			



subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Spinal fracture subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Tick bite subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Vascular access complication subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	3 / 199 (1.51%) 3	6 / 199 (3.02%) 6	
Atrial flutter subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	3 / 199 (1.51%) 3	
Automatic defibrillator implantation (accidental) subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Chest pain - cardiac subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	0 / 199 (0.00%) 0	
Heart failure subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Palpitations subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	2 / 199 (1.01%) 2	
Paroxysmal auricular fibrillation subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Pericardial effusion			

subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	1 / 199 (0.50%) 1	
Sinus bradycardia subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	2 / 199 (1.01%) 2	
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	7 / 199 (3.52%) 7	
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Nervous system disorders			
Acute flaccid paraparesis (from the clavicles down) subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Amnesia subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Anosmia subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	0 / 199 (0.00%) 0	
Balance issues subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Cognitive disturbance subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Concentration impairment subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Depressed level of consciousness subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Dizziness			

subjects affected / exposed	8 / 199 (4.02%)	12 / 199 (6.03%)
occurrences (all)	8	12
Dysesthesia		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Dysgeusia		
subjects affected / exposed	27 / 199 (13.57%)	17 / 199 (8.54%)
occurrences (all)	27	17
Faint		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Headache		
subjects affected / exposed	23 / 199 (11.56%)	22 / 199 (11.06%)
occurrences (all)	23	22
Ischemia cerebrovascular		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Lethargy		
subjects affected / exposed	5 / 199 (2.51%)	2 / 199 (1.01%)
occurrences (all)	5	2
Memory impairment		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Movements involuntary		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Neuralgia		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Nystagmus		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Paresthesia		
subjects affected / exposed	5 / 199 (2.51%)	4 / 199 (2.01%)
occurrences (all)	5	4
Peripheral motor neuropathy		

subjects affected / exposed	2 / 199 (1.01%)	3 / 199 (1.51%)	
occurrences (all)	2	3	
Peripheral sensory neuropathy			
subjects affected / exposed	8 / 199 (4.02%)	2 / 199 (1.01%)	
occurrences (all)	8	2	
Presyncope			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Ride instability			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Seizure			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences (all)	2	1	
Spasticity			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Torticollis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	3 / 199 (1.51%)	2 / 199 (1.01%)	
occurrences (all)	3	2	
Trigeminal nerve disorder			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences (all)	2	0	
Vasovagal reaction			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			

Anemia			
subjects affected / exposed	68 / 199 (34.17%)	69 / 199 (34.67%)	
occurrences (all)	68	69	
Cytolysis Eosinophilia			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Febrile neutropenia			
subjects affected / exposed	6 / 199 (3.02%)	3 / 199 (1.51%)	
occurrences (all)	6	3	
Hemolysis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Hypovolemic shock			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences (all)	2	0	
Lymph node pain			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Neutrophilia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Thrombocytosis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear discharge (right)			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Ear pain			

subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	1 / 199 (0.50%) 1	
Hearing impaired subjects affected / exposed occurrences (all)	3 / 199 (1.51%) 3	1 / 199 (0.50%) 1	
Hyperacusis subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Tinnitus subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	4 / 199 (2.01%) 4	
Vertigo subjects affected / exposed occurrences (all)	5 / 199 (2.51%) 5	3 / 199 (1.51%) 3	
Eye disorders (Hyper)sensitive eyes subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	0 / 199 (0.00%) 0	
Blurred vision subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	2 / 199 (1.01%) 2	
Cataract subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	1 / 199 (0.50%) 1	
Diplopia subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Dry eye subjects affected / exposed occurrences (all)	12 / 199 (6.03%) 12	7 / 199 (3.52%) 7	
Eye discharge subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Eye herpes (right) subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	

Eye irritation		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Eye pain		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Eyelid function disorder		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Flashing lights		
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)
occurrences (all)	0	2
Floaters		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Full thickness macular hole (right)		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Glaucoma		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Gritty eyes		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Hyperopia		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Hyposfagma (right eye)		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Inferotemporal nevus eye (left)		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Keratitis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1

Redness eye (left)			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Vision decreased			
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)	
occurrences (all)	0	2	
Visual acuity loss			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Visual impairment			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Watering eyes			
subjects affected / exposed	17 / 199 (8.54%)	25 / 199 (12.56%)	
occurrences (all)	17	25	
Gastrointestinal disorders			
Abdomen sensibility			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Abdominal cramps			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	22 / 199 (11.06%)	15 / 199 (7.54%)	
occurrences (all)	22	15	
Anal fissure			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences (all)	2	0	
Anal fistula			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Anal hemorrhage			



subjects affected / exposed	3 / 199 (1.51%)	1 / 199 (0.50%)
occurrences (all)	3	1
Anal mucositis		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Anal pain		
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)
occurrences (all)	0	2
Ascites		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Belching		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Bloating		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Colitis		
subjects affected / exposed	6 / 199 (3.02%)	1 / 199 (0.50%)
occurrences (all)	6	1
Constipation		
subjects affected / exposed	82 / 199 (41.21%)	80 / 199 (40.20%)
occurrences (all)	82	80
Dental caries		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Diarrhea		
subjects affected / exposed	55 / 199 (27.64%)	39 / 199 (19.60%)
occurrences (all)	55	39
Diverticulitis		
subjects affected / exposed	3 / 199 (1.51%)	0 / 199 (0.00%)
occurrences (all)	3	0
Dry mouth		
subjects affected / exposed	8 / 199 (4.02%)	8 / 199 (4.02%)
occurrences (all)	8	8
Dyspepsia		

subjects affected / exposed	7 / 199 (3.52%)	7 / 199 (3.52%)
occurrences (all)	7	7
Dysphagia		
subjects affected / exposed	9 / 199 (4.52%)	8 / 199 (4.02%)
occurrences (all)	9	8
Epigastralgia		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Esophageal pain		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Fecal incontinence		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	1 / 199 (0.50%)	2 / 199 (1.01%)
occurrences (all)	1	2
Food poisoning		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Gastric hemorrhage		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Gastric ulcer		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Gastritis		
subjects affected / exposed	5 / 199 (2.51%)	2 / 199 (1.01%)
occurrences (all)	5	2
Gastroesophageal reflux disease		
subjects affected / exposed	8 / 199 (4.02%)	11 / 199 (5.53%)
occurrences (all)	8	11
Gastrointestinal pain		
subjects affected / exposed	2 / 199 (1.01%)	4 / 199 (2.01%)
occurrences (all)	2	4
Gingival hyperplasia		

subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Gingival pain		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Glossitis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Hemorrhoidal hemorrhage		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Hemorrhoids		
subjects affected / exposed	7 / 199 (3.52%)	7 / 199 (3.52%)
occurrences (all)	7	7
Hernia		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Hiatus hernia		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Inguinal hernia		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Mouth sores		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Mouth ulcer		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Mucositis oral		
subjects affected / exposed	65 / 199 (32.66%)	47 / 199 (23.62%)
occurrences (all)	65	47
Nausea		
subjects affected / exposed	84 / 199 (42.21%)	93 / 199 (46.73%)
occurrences (all)	84	93
Odynophagia		

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Oral dysesthesia		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Oral hemorrhage		
subjects affected / exposed	3 / 199 (1.51%)	2 / 199 (1.01%)
occurrences (all)	3	2
Oral pain		
subjects affected / exposed	5 / 199 (2.51%)	1 / 199 (0.50%)
occurrences (all)	5	1
Pancreatitis		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Periodontal disease		
subjects affected / exposed	5 / 199 (2.51%)	0 / 199 (0.00%)
occurrences (all)	5	0
Proctitis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Pyrosis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Rectal hemorrhage		
subjects affected / exposed	4 / 199 (2.01%)	2 / 199 (1.01%)
occurrences (all)	4	2
Rectal pain		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Retching		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Salivary duct inflammation		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Stomach pain		

subjects affected / exposed occurrences (all)	6 / 199 (3.02%) 6	5 / 199 (2.51%) 5	
Stomatitis subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	0 / 199 (0.00%) 0	
Teeth sensibility subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	7 / 199 (3.52%) 7	1 / 199 (0.50%) 1	
Umbilical hernia subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Upper gastrointestinal hemorrhage subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	30 / 199 (15.08%) 30	28 / 199 (14.07%) 28	
Hepatobiliary disorders Cholangitis subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Hepatic pain subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Intrahepatic bile ducts/common bile duct dilatation subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Skin and subcutaneous tissue disorders Actinic keratosis eyelid (right) subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Alopecia			

subjects affected / exposed	5 / 199 (2.51%)	9 / 199 (4.52%)
occurrences (all)	5	9
Angular cheilitis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Body odor		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Bullous dermatitis		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Cellulitis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Corner mouth subcutaneous swelling		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Cutaneous eruption		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Cutaneous erythema		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Dry skin		
subjects affected / exposed	18 / 199 (9.05%)	7 / 199 (3.52%)
occurrences (all)	18	7
Eczema		
subjects affected / exposed	5 / 199 (2.51%)	2 / 199 (1.01%)
occurrences (all)	5	2
Erythema		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Erythema multiforme		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Erythromatosis finger lesion (left)		

subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Eschar		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Exfoliative dermatitis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Face cutaneous toxicity		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Face erythema		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Folliculitis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Hyperhidrosis		
subjects affected / exposed	10 / 199 (5.03%)	3 / 199 (1.51%)
occurrences (all)	10	3
Leg skin tear		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Lower leg red spot (right)		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Nail changes		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Nail fingers erythema		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Nasal mucositis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Neck spots		

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Nodular skin elbows erythema		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Non-pruginous erythematous muscle lesion (right)		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Pain of skin		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)
occurrences (all)	0	2
Penis erosions		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Pharyngeal erythema		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Pityriasis versicolor		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Pruritus		
subjects affected / exposed	35 / 199 (17.59%)	24 / 199 (12.06%)
occurrences (all)	35	24
Psoriasis		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Rash		
subjects affected / exposed	4 / 199 (2.01%)	4 / 199 (2.01%)
occurrences (all)	4	4
Rash acneiform		



subjects affected / exposed	11 / 199 (5.53%)	6 / 199 (3.02%)
occurrences (all)	11	6
Rash maculo-papular		
subjects affected / exposed	35 / 199 (17.59%)	18 / 199 (9.05%)
occurrences (all)	35	18
Rosacea		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Scalp pain		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Scalp spots		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Scleroderma		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Shin itching		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Skin atrophy		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Skin hyperpigmentation		
subjects affected / exposed	4 / 199 (2.01%)	1 / 199 (0.50%)
occurrences (all)	4	1
Skin hypopigmentation		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Skin toxicity		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Skin ulceration		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Stoma site irritation		

subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	4 / 199 (2.01%) 4	
Venous eczema subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Wart lesions subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Renal and urinary disorders			
Acute kidney disease subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Acute kidney injury subjects affected / exposed occurrences (all)	4 / 199 (2.01%) 4	1 / 199 (0.50%) 1	
Chronic kidney disease subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	2 / 199 (1.01%) 2	
Creatinine clearance decreased subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	1 / 199 (0.50%) 1	
Cystitis noninfective subjects affected / exposed occurrences (all)	2 / 199 (1.01%) 2	0 / 199 (0.00%) 0	
Dysuria subjects affected / exposed occurrences (all)	6 / 199 (3.02%) 6	4 / 199 (2.01%) 4	
Estimated glomerular filtration rate (eGFR) decreased subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Glomerular filtration rate decreased			

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Glomerulonephritis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Hematuria		
subjects affected / exposed	8 / 199 (4.02%)	2 / 199 (1.01%)
occurrences (all)	8	2
Nephritis		
subjects affected / exposed	4 / 199 (2.01%)	0 / 199 (0.00%)
occurrences (all)	4	0
Nocturia		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Proteinuria		
subjects affected / exposed	33 / 199 (16.58%)	21 / 199 (10.55%)
occurrences (all)	33	21
Renal calculi		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Renal failure		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Renal function deterioration		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Renal impairment		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Renal toxicity		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Urine ketones high levels		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Urethra bleeding		

subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Urethra burning subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Urinary flow change subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Urinary frequency subjects affected / exposed occurrences (all)	5 / 199 (2.51%) 5	6 / 199 (3.02%) 6	
Urinary retention subjects affected / exposed occurrences (all)	6 / 199 (3.02%) 6	2 / 199 (1.01%) 2	
Urinary symptoms subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Urine offensive smell subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Endocrine disorders Diabetes (type II) subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0	
Hyperparathyroidism subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1	
Hyperthyroidism subjects affected / exposed occurrences (all)	13 / 199 (6.53%) 13	3 / 199 (1.51%) 3	
Hypothyroidism subjects affected / exposed occurrences (all)	23 / 199 (11.56%) 23	5 / 199 (2.51%) 5	
Musculoskeletal and connective tissue disorders			

Arthralgia		
subjects affected / exposed	25 / 199 (12.56%)	20 / 199 (10.05%)
occurrences (all)	25	20
Arthritis		
subjects affected / exposed	5 / 199 (2.51%)	1 / 199 (0.50%)
occurrences (all)	5	1
Back pain		
subjects affected / exposed	24 / 199 (12.06%)	17 / 199 (8.54%)
occurrences (all)	24	17
Bone pain		
subjects affected / exposed	7 / 199 (3.52%)	5 / 199 (2.51%)
occurrences (all)	7	5
Bursitis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Calf swelling (right)		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Chest wall pain		
subjects affected / exposed	5 / 199 (2.51%)	13 / 199 (6.53%)
occurrences (all)	5	13
Compression inferior limb sensitivity		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Flank pain		
subjects affected / exposed	10 / 199 (5.03%)	9 / 199 (4.52%)
occurrences (all)	10	9
Generalized muscle weakness		
subjects affected / exposed	1 / 199 (0.50%)	3 / 199 (1.51%)
occurrences (all)	1	3
Hemithoracic tenderness (right)		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Ilical pain		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0

Joint effusion		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Joint range of motion decreased		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Maxillary/ mandibular bones alveolar lysis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Muscle cramp		
subjects affected / exposed	4 / 199 (2.01%)	1 / 199 (0.50%)
occurrences (all)	4	1
Muscle weakness lower limb		
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)
occurrences (all)	2	0
Muscle weakness upper limb		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Muscular pain		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Myalgia		
subjects affected / exposed	15 / 199 (7.54%)	2 / 199 (1.01%)
occurrences (all)	15	2
Neck pain		
subjects affected / exposed	9 / 199 (4.52%)	5 / 199 (2.51%)
occurrences (all)	9	5
Osteoporosis		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Pain in extremity		
subjects affected / exposed	18 / 199 (9.05%)	11 / 199 (5.53%)
occurrences (all)	18	11
Polimialgia arthralgic		

subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Polyalgia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Rotator cuff injury			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Sciatalgia			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Shoulder pain			
subjects affected / exposed	1 / 199 (0.50%)	3 / 199 (1.51%)	
occurrences (all)	1	3	
Shoulder pain (right)			
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)	
occurrences (all)	1	1	
Tendonitis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)	
occurrences (all)	0	1	
Infections and infestations			
Bladder infection			
subjects affected / exposed	2 / 199 (1.01%)	0 / 199 (0.00%)	
occurrences (all)	2	0	
Bronchial infection			
subjects affected / exposed	4 / 199 (2.01%)	4 / 199 (2.01%)	
occurrences (all)	4	4	
COVID-19 infection			
subjects affected / exposed	17 / 199 (8.54%)	10 / 199 (5.03%)	
occurrences (all)	17	10	
Candidiasis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Catheter related infection			
subjects affected / exposed	0 / 199 (0.00%)	2 / 199 (1.01%)	
occurrences (all)	0	2	

Cold		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Conjunctivitis		
subjects affected / exposed	13 / 199 (6.53%)	6 / 199 (3.02%)
occurrences (all)	13	6
Dental abscess		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Dental phlegmon		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Device related infection		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Dorsal boil		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Enterocolitis infectious		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Esophageal infection		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Eye infection		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Fungemia		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Gastroenteritis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Gum infection		
subjects affected / exposed	0 / 199 (0.00%)	4 / 199 (2.01%)
occurrences (all)	0	4



Herpes simplex reactivation subjects affected / exposed occurrences (all)	4 / 199 (2.01%) 4	1 / 199 (0.50%) 1
Infected big toe (right) subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1
Infection (unknown source) subjects affected / exposed occurrences (all)	3 / 199 (1.51%) 3	0 / 199 (0.00%) 0
Kidney infection subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Laryngitis subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Lip infection subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Lung infection subjects affected / exposed occurrences (all)	6 / 199 (3.02%) 6	13 / 199 (6.53%) 13
Lymph gland infection subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	0 / 199 (0.00%) 0
Mouth abcess subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1
Mucosal infection subjects affected / exposed occurrences (all)	4 / 199 (2.01%) 4	4 / 199 (2.01%) 4
Nail infection subjects affected / exposed occurrences (all)	1 / 199 (0.50%) 1	1 / 199 (0.50%) 1
Otitis media subjects affected / exposed occurrences (all)	0 / 199 (0.00%) 0	1 / 199 (0.50%) 1

Papulopustular rash		
subjects affected / exposed	3 / 199 (1.51%)	0 / 199 (0.00%)
occurrences (all)	3	0
Penile infection		
subjects affected / exposed	3 / 199 (1.51%)	1 / 199 (0.50%)
occurrences (all)	3	1
Pleural infection		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Port infection		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Prostate infection		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Pyrexia		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Rash pustular		
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)
occurrences (all)	2	1
Rhinitis infective		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Sepsis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Shingles		
subjects affected / exposed	3 / 199 (1.51%)	2 / 199 (1.01%)
occurrences (all)	3	2
Sialoadenitis		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Sinusitis		
subjects affected / exposed	2 / 199 (1.01%)	3 / 199 (1.51%)
occurrences (all)	2	3

Skin infection			
subjects affected / exposed	8 / 199 (4.02%)	6 / 199 (3.02%)	
occurrences (all)	8	6	
Soft tissue infection			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Staphylococcus Aureus infection			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Thrush			
subjects affected / exposed	8 / 199 (4.02%)	7 / 199 (3.52%)	
occurrences (all)	8	7	
Tonsillitis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	8 / 199 (4.02%)	6 / 199 (3.02%)	
occurrences (all)	8	6	
Upper respiratory infection			
subjects affected / exposed	9 / 199 (4.52%)	7 / 199 (3.52%)	
occurrences (all)	9	7	
Urinary tract infection			
subjects affected / exposed	19 / 199 (9.55%)	8 / 199 (4.02%)	
occurrences (all)	19	8	
Wound infection			
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)	
occurrences (all)	2	2	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	58 / 199 (29.15%)	54 / 199 (27.14%)	
occurrences (all)	58	54	
Dehydration			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Hypercalcemia			

subjects affected / exposed	13 / 199 (6.53%)	11 / 199 (5.53%)
occurrences (all)	13	11
Hyperglycemia		
subjects affected / exposed	13 / 199 (6.53%)	11 / 199 (5.53%)
occurrences (all)	13	11
Hyperkalemia		
subjects affected / exposed	4 / 199 (2.01%)	4 / 199 (2.01%)
occurrences (all)	4	4
Hyperlipidemia		
subjects affected / exposed	0 / 199 (0.00%)	1 / 199 (0.50%)
occurrences (all)	0	1
Hypermagnesemia		
subjects affected / exposed	2 / 199 (1.01%)	2 / 199 (1.01%)
occurrences (all)	2	2
Hypernatremia		
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)
occurrences (all)	1	0
Hyperphosphatemia		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Hypertriglyceridemia		
subjects affected / exposed	1 / 199 (0.50%)	1 / 199 (0.50%)
occurrences (all)	1	1
Hyperuricemia		
subjects affected / exposed	8 / 199 (4.02%)	4 / 199 (2.01%)
occurrences (all)	8	4
Hypoalbuminemia		
subjects affected / exposed	6 / 199 (3.02%)	4 / 199 (2.01%)
occurrences (all)	6	4
Hypocalcemia		
subjects affected / exposed	6 / 199 (3.02%)	1 / 199 (0.50%)
occurrences (all)	6	1
Hypokalemia		
subjects affected / exposed	8 / 199 (4.02%)	6 / 199 (3.02%)
occurrences (all)	8	6
Hypomagnesemia		

subjects affected / exposed	18 / 199 (9.05%)	27 / 199 (13.57%)	
occurrences (all)	18	27	
Hyponatremia			
subjects affected / exposed	9 / 199 (4.52%)	2 / 199 (1.01%)	
occurrences (all)	9	2	
Hypophosphatemia			
subjects affected / exposed	2 / 199 (1.01%)	1 / 199 (0.50%)	
occurrences (all)	2	1	
Hypoproteinemia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	
Zinc deficiency			
subjects affected / exposed	1 / 199 (0.50%)	0 / 199 (0.00%)	
occurrences (all)	1	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2020	<p>The protocol has been updated to account for the new safety information for atezolizumab, including the addition of the newly identified risks of immune-mediated myositis and immune-mediated nephritis. The Management of atezolizumab related toxicities has been updated based on the latest version of the atezolizumab IB Version 15, July 2019, the Addendum 2, December 2019 to the IB V15 and the diagnostic criteria and management guidelines for haemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS) replacing systemic immune activation (SIS) communicated by Roche separately through a Safety Memo.</p> <p>In addition, the list of AESIs have been updated to reflect the new safety information and active autoimmune disease that required systemic treatment in the past 2 year as well as history of active diverticulitis have been added as exclusion criteria.</p> <p>Furthermore, some minor protocol clarifications have been added and some ambiguities and typos eliminated.</p>
10 May 2021	<p>The protocol is being amended to change the primary endpoint from a co-primary endpoint of overall survival (OS) and progression free survival (PFS) to overall survival only. This change is associated with an increase in sample size to a total of 400 randomized patients.</p> <p>Several adaptations were made throughout the protocol to account for the change to OS as primary endpoint, the resulting samples size increase and the adaptation of the trial duration.</p>
03 May 2024	<p>The protocol is being amended to include the option for the treatment beyond trial closure through the F. Hoffmann-La Roche Ltd. Post-Trial Access Programme (PTAP). The description of this PTAP option has been added as a separate subsection to Section 9.</p> <p>In addition, several formatting changes were made throughout the protocol to account for the change in the sponsor name, as notified earlier.</p>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported