Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Niraparib Maintenance Treatment in Patients with Advanced Ovarian Cancer Following Response on Front-Line Platinum-Based Chemotherapy

Summary

EudraCT number	2015-000952-11
Trial protocol	FI DK NO BE SE IE DE FR GB HU CZ PL IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	20 May 2020
First version publication date	20 May 2020

Trial information

Trial identification

Sponsor protocol code	213359

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	30 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of niraparib versus placebo as maintenance treatment, as measured by progression-free survival (PFS), in participants with Stage III or IV ovarian cancer (including fallopian and peritoneal cancers) with a complete response (CR) or partial response (PR) following front-line platinumbased chemotherapy treatment.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 July 2016
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	Canada: 87
Country: Number of subjects enrolled	United States: 246
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	Ukraine: 29
Country: Number of subjects enrolled	Belgium: 40
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	Denmark: 24
Country: Number of subjects enrolled	Spain: 95
Country: Number of subjects enrolled	Finland: 11
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Israel: 17
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Sweden: 2
Worldwide total number of subjects	733
EEA total number of subjects	316

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)	444
From 65 to 84 years	287
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This was a double-blind, randomized, placebo-controlled study in participants with Stage III or IV ovarian cancer. Participants were randomized to receive either niraparib or placebo in a 2:1 ratio. The results of the study are based on primary analysis (up to 34 months).

Pre-assignment

Screening details:

A total of 989 participants were screened, of which 256 participants did not meet eligibility criteria. A total of 733 participants were enrolled and randomized in the study, of which 728 participants received study treatment (4 participants were screen failures after randomization and 1 participant withdrew consent before first dose).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matching niraparib 300 milligram (mg) (3×100 mg capsules) (fixed dose) once daily (QD) orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received placebo based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kilogram [kg] and Baseline platelet count >=150,000 per microliter [µL]) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants received placebo matching niraparib 300 milligram (mg) (3×100 mg capsules) (fixed dose) once daily (QD) orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received placebo based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kilogram (kg) and Baseline platelet count >=150,000 per microliter [µL]) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).

Arm title	Niraparib

Arm description:

Participants received niraparib 300 mg (3×100 mg capsules) (fixed dose) QD orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received niraparib based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kg and Baseline platelet count >=150,000 per µL) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).

Arm type	Experimental
Investigational medicinal product name	Niraparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants received niraparib 300 mg (3×100 mg capsules) (fixed dose) QD orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received niraparib based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kg and Baseline platelet count >=150,000 per µL) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).

Number of subjects in period 1	Placebo	Niraparib
Started	246	487
Received study treatment	244	484
Completed	191	397
Not completed	55	90
Adverse event, serious fatal	30	48
Consent withdrawn by subject	18	36
Disease progression	6	4
Site closed	-	1
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching niraparib 300 milligram (mg) (3×100 mg capsules) (fixed dose) once daily (QD) orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received placebo based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kilogram [kg] and Baseline platelet count >=150,000 per microliter [µL]) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).	
Reporting group title	Niraparib
Reporting group description:	
Participants received niraparib 300 mg (3×100 mg capsules) (fixed dose) QD orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received niraparib based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kg and Baseline platelet count >=150,000 per µL) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).	

Reporting group values	Placebo	Niraparib	Total
Number of subjects	246	487	733
Age categorical Units: Subjects			
Total participants	246	487	733
Age Continuous Units: Years			
arithmetic mean	61.3	61.1	
standard deviation	± 10.39	± 10.79	-
Sex: Female, Male Units: Participants			
Female	246	487	733
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
White	219	436	655
Black	2	10	12
Asian	11	14	25
American Indian or Alaska Native	0	1	1
Native Hawaiian or other Pacific Islander	0	1	1
Unknown	14	25	39

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo matching niraparib 300 milligram (mg) (3×100 mg capsules) (fixed dose) once daily (QD) orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received placebo based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kilogram [kg] and Baseline platelet count >=150,000 per microliter [µL]) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).

Reporting group title	Niraparib

Reporting group description:

Participants received niraparib 300 mg (3×100 mg capsules) (fixed dose) QD orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received niraparib based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kg and Baseline platelet count >=150,000 per µL) or 200 mg (2×100 mg capsules for participants with a Baseline body weight <77 kg or Baseline platelet count <150,000 per µL).

Primary: Progression free survival

End point title	Progression free survival

End point description:

Progression free survival was defined as the time from the date of treatment randomization to the date of first documentation of disease progression or death due to any cause in the absence of documented progression, whichever occurs first. It was assessed by the blinded independent central review (BICR). Median and 95% confidence interval (CI) are presented. Intent-to-Treat (ITT) population comprised of all participants who were randomized into the study.

End point type	Primary

End point timeframe:

Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[1]	487[2]		
Units: Months				
median (confidence interval 95%)	8.2 (7.3 to 8.5)	13.8 (11.5 to 14.9)		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo.

Comparison groups	Placebo v Niraparib

Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.502
upper limit	0.755

Notes:

[3] - p-value was calculated based on stratified log-rank test using randomization stratification factors: administration of neoadjuvant chemotherapy, best response to platinum therapy and homologous recombination deficiency (HRD) status.

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from the date of randomization to the date of death by any cause. Median and 95% CI are presented for overall survival interim analysis. 99999 indicates, median and 95% CI (upper limit) could not be derived, as <50% of participants experienced the event within the treatment arm. 88888 indicates, 95% CI (upper limit) could not be derived, as <75% of participants experienced the event within the treatment arm.

End point type	Secondary

End point timeframe:

Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[4]	487[5]		
Units: Months				
median (confidence interval 95%)	99999 (25.0 to 99999)	30.3 (30.3 to 88888)		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo.

Comparison groups	Placebo v Niraparib

Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1238 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.442
upper limit	1.106

Notes:

[6] - p-value was calculated based on stratified log-rank test using randomization stratification factors: administration of neoadjuvant chemotherapy, best response to platinum therapy and HRD status.

Secondary: Time to first subsequent therapy (TFST)

End point title	Time to first subsequent therapy (TFST)

End point description:

Time to first subsequent therapy was defined as the time from the date of randomization to the date of the first subsequent anti-cancer therapy or death, whichever occurs first. Median and 95% CI are presented.

End point type	Secondary

End point timeframe:

Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[7]	487[8]		
Units: Months				
median (confidence interval 95%)	12.0 (10.3 to 13.9)	18.6 (15.8 to 24.7)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo.

Comparison groups	Placebo v Niraparib
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [9]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.521
upper limit	0.802

Notes:

[9] - p-value was calculated based on stratified log-rank test using randomization stratification factors: administration of neoadjuvant chemotherapy, best response to platinum therapy and HRD status.

Secondary: Progression-Free Survival-2 (PFS2)

End point title	Progression-Free Survival-2 (PFS2)

End point description:

PFS2 was defined as the time from the date of randomization to the date of progression on the next anti-cancer therapy following study treatment or death by any cause, whichever occurs first. Median and 95% CI are presented. 99999 indicates, median and 95% CI could not be derived, as <25% of participants experienced the event within the treatment arm. 88888 indicates, 95% CI (upper limit) could not be derived, as <75% of participants experienced the event within the treatment arm.

End point type	Secondary

End point timeframe:

Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[10]	487[11]		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	27.2 (25.3 to 88888)		

Notes:

[10] - ITT Population

[11] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo.

Comparison groups	Placebo v Niraparib
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2242 [12]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.577
upper limit	1.139

Notes:

[12] - p-value was calculated based on stratified log-rank test using randomization stratification factors: administration of neoadjuvant chemotherapy, best response to platinum therapy and HRD status.

Secondary: Change from Baseline in participant reported outcome (PRO): Functional Assessment of Cancer Therapy-Ovarian Symptom Index (FOSI)

End point title	Change from Baseline in participant reported outcome (PRO): Functional Assessment of Cancer Therapy-Ovarian Symptom Index (FOSI)

End point description:

FOSI is a validated, 8-item measure of symptom response to treatment for ovarian cancer. Participants responded to their symptom experience over the past 7 days using a 5-point Likert scale scored from "not at all" (0) to "very much" (4). FOSI score was calculated as (sum of item scores)*8 divided by (number of items answered). The FOSI score ranged from 0 (severely symptomatic) to 32 (asymptomatic). A higher score indicated a better quality of life (QoL). Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to Week 24

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240[13]	479[14]		
Units: Scores on a scale				
least squares mean (standard error)	-0.3 (± 0.22)	-0.4 (± 0.15)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PRO: European quality of life scale, 5-dimensions, 5-levels of severity (EQ-5D-5L) utility score

End point title	Change from Baseline in PRO: European quality of life scale, 5-dimensions, 5-levels of severity (EQ-5D-5L) utility score

End point description:

The EQ-5D-5L is a health-related QoL instrument. The 5-item measure has 1 question assessing each of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression and 5 levels for each dimension including 1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems & 5=extreme problems. The health state is combining the levels of answers from each of the 5 questions. Each health state is referred to in terms of a 5 digit code. Health state 5 digit code is translated into utility score, which is valued up to 1 (perfect health) with lower values meaning worse state. EQ-5D-5L utility score ranges from -0.281 to 1. Higher scores indicate better health. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1). Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to Week 24

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243[15]	477[16]		
Units: Scores on a scale				
least squares mean (standard error)	0.005 (± 0.0066)	0.016 (± 0.0046)		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in functional scales of European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30)

End point title	Change from Baseline in functional scales of European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30)

End point description:

EORTC-QLQ-C30 incorporates 5 functional scales (physical, role, cognitive, emotional, and social) assessing additional symptoms commonly reported by participants with cancer. 5 functional scales had total 15 items (physical-5, role-2, cognitive-4, emotional-2, and social-2). Each functional scales score was calculated by averaging scores of all scale items and transforming average scores linearly (1 minus [average score minus 1] divided by 3*100). All of the functional scales range in score from 0 to 100. Higher score represents a higher ("better") level of functioning. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to Week 24

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[17]	479[18]		
Units: Scores on a scale				
least squares mean (standard error)				
Physical Functioning, n=244,479	2.119 (± 0.8131)	2.013 (± 0.5735)		
Role Functioning, n=244,479	2.341 (± 1.2427)	1.590 (± 0.8810)		
Emotional Functioning, n=243,478	-0.011 (± 1.1218)	-0.870 (± 0.7685)		
Cognitive Functioning, n=243,478	-0.020 (± 1.2105)	-0.842 (± 0.7952)		
Social Functioning, n=243,478	5.557 (± 1.2449)	4.445 (± 0.8633)		

Notes:

[17] - ITT Population

[18] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in global health status/QoL of EORTC-QLQ-C30

End point title	Change from Baseline in global health status/QoL of EORTC-QLQ-C30

End point description:

EORTC-QLQ-C30 incorporates a global health status/QoL scale (global health status, QoL) assessing additional symptoms commonly reported by participants with cancer. A global health status/QoL scale had total 2 items. Each global health status/QoL scales score was calculated by averaging scores of all scale items and transforming average scores linearly ([average score minus 1] divided by 6*100). The global health status/QoL scales range in score from 0 to 100. Higher score represents a higher ("better") level of health status/QoL. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to Week 24

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243[19]	478[20]		
Units: Scores on a scale				
least squares mean (standard error)	1.177 (± 1.0005)	1.009 (± 0.6898)		

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in symptoms scales and symptoms items (dyspnea, appetite loss, insomnia, constipation, diarrhea and financial difficulty) of EORTC-QLQ-C30

End point title	Change from Baseline in symptoms scales and symptoms items (dyspnea, appetite loss, insomnia, constipation, diarrhea and financial difficulty) of EORTC-QLQ-C30

End point description:

EORTC-QLQ-C30 incorporates 3 symptom scales (fatigue, pain, and nausea/vomiting), and 6 single items assessing additional symptoms commonly reported by participants with cancer. Symptom scale had total 7 items (fatigue-3, pain-2, nausea/vomiting-2). Each symptoms scales and 6 single additional symptoms items score was calculated by averaging scores of all scale items and transforming average scores linearly ([average score minus 1] divided by 3*100). All of the symptoms scales and 6 single additional symptoms scales range in score from 0 to 100. Higher score represents a higher ("worse")

level of symptoms. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles). 99999 indicates data is not estimable due to insufficient model fit.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to Week 24

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[21]	480[22]		
Units: Scores on a scale				
least squares mean (standard error)				
Fatigue, n=243,479	-0.082 (± 1.2394)	0.085 (± 0.8363)		
Nausea/Vomiting, n=244,479	1.673 (± 0.7595)	3.115 (± 0.4828)		
Pain, n=244,480	-0.195 (± 1.2274)	0.765 (± 1.0166)		
Dyspnea, n=244,479	0.644 (± 1.3592)	1.347 (± 0.8518)		
Insomnia, n=244,479	2.195 (± 1.9882)	3.478 (± 1.2791)		
Appetite Loss, n=244,479	99999 (± 99999)	99999 (± 99999)		
Constipation, n=244,478	-1.147 (± 1.5793)	6.356 (± 1.0446)		
Diarrhea, n=243,478	99999 (± 99999)	99999 (± 99999)		
Financial Difficulties, n=243,475	-5.058 (± 1.2978)	-3.356 (± 0.9276)		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in functional scales of European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module (EORTC-QLQ-OV28)

End point title	Change from Baseline in functional scales of European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Ovarian Cancer Module (EORTC-QLQ-OV28)

End point description:

EORTC-QLQ-OV28 is supplement to EORTC-QLQ-C30. It includes 3 functional scales (body image, sexuality, attitude to disease/treatment). Functional scales score (body Image and attitude to disease/treatment) was calculated by averaging scores of all scale items and transforming average scores linearly (1 minus [average score minus 1] divided by 3*100). Functional scales score (sexuality) was calculated by averaging scores of all scale items and transforming average scores linearly ([average score minus 1] divided by 3*100). All of the functional scales range in score from 0 to 100. Higher score represents a higher (“better”) level of functioning. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[23]	475[24]		
Units: Scores on a scale				
least squares mean (standard error)				
Body Image, n=244,475	10.069 (± 1.4820)	8.488 (± 1.0138)		
Sexuality, n=240,471	3.257 (± 1.1886)	3.625 (± 0.8004)		
Attitude to disease/Treatment, n=244,475	12.216 (± 1.3257)	13.660 (± 0.9309)		

Notes:

[23] - ITT Population

[24] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in symptoms scale of EORTC-QLQ-OV28

End point title	Change from Baseline in symptoms scale of EORTC-QLQ-OV28

End point description:

EORTC-QLQ-OV28 is supplement to EORTC-QLQ-C30. It includes 3 functional scales (body image, sexuality, attitude to disease/treatment) and 5 symptom scales/items (abdominal/GI symptoms, peripheral neuropathy, hormonal/menopausal symptoms, other chemotherapy side-effects, and hair loss). Symptoms scales score was calculated by averaging scores of all scale items and transforming average scores linearly ([average score minus 1] divided by 3*100). All of the symptoms scales range in score from 0 to 100. Higher score represents a higher (“worse”) level of symptoms. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose) and Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[25]	481[26]		
Units: Scores on a scale				
least squares mean (standard error)				
Abdominal/GI, n=244,481	0.832 (± 0.8110)	2.185 (± 0.5703)		
Peripheral Neuropathy, n=244,480	-9.629 (± 1.3219)	-8.217 (± 0.9295)		
Hormonal/Menopausal Symptoms, n=244,480	-2.521 (± 1.3074)	1.501 (± 0.8803)		

Other Chemotherapy Side Effects, n=244,480	-3.023 (± 0.8358)	-2.219 (± 0.5581)		
Hair Loss, n=242,477	-20.743 (± 1.3690)	-23.363 (± 0.9821)		

Notes:

[25] - ITT Population

[26] - ITT Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of participants with any non-serious adverse event (non-SAE) or any SAE

End point title	Number of participants with any non-serious adverse event (non-SAE) or any SAE

End point description:

An adverse event is any untoward medical occurrence that occurs in a participant or clinical investigation participant administered a pharmaceutical product, and which does not necessarily have to have a causal relationship with study treatment. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly or birth defect or any other situation according to medical or scientific judgment was categorized as SAE. Safety Population comprised of all participants who received at least 1 dose of study drug. 5 participants (2 participants from Placebo group and 3 participants from Niraparib group) out of 733 participants did not receive any study treatment and thus, were excluded from the Safety Population.

End point type	Other pre-specified

End point timeframe:

Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[27]	484[28]		
Units: Participants				
Any non-SAE	223	478		
Any SAE	32	156		

Notes:

[27] - Safety Population

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area Under the Curve (AUC) from 0 to the last quantifiable concentration (AUC[0-last])

End point title	Area Under the Curve (AUC) from 0 to the last quantifiable concentration (AUC[0-last])[29]

End point description:

Blood samples were planned to be collected for assessment of AUC(0-last). This was an other pre-specified outcome measure. Data will not be analyzed and reported.

End point type	Other pre-specified

End point timeframe:

Up to 34 months

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	0[30]			
Units: Hours*nanogram per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[30] - ITT Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Peak plasma concentration (Cmax)

End point title	Peak plasma concentration (Cmax)[31]

End point description:

Blood samples were planned to be collected for assessment of Cmax. This was an other pre-specified outcome measure. Data will not be analyzed and reported.

End point type	Other pre-specified

End point timeframe:

Up to 34 months

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	0[32]			
Units: Nanograms per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[32] - ITT Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of participants with positive HRD test

End point title	Number of participants with positive HRD test

End point description:

Number of participants with positive HRD test was planned to be assessed. This was an other pre-specified outcome measure. Data will not be analyzed and reported.

End point type	Other pre-specified

End point timeframe:

Up to 34 months

End point values	Placebo	Niraparib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[33]	0[34]		
Units: Participants				

Notes:

[33] - ITT Population

[34] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-SAEs were reported from start of study treatment (Day 1) and up to 34 months

Adverse event reporting additional description:

Non-SAEs and SAEs were presented for Safety Population. 5 participants out of 733 participants did not receive any study treatment and thus, were excluded from the Safety Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo matching niraparib 300 milligram (mg) (3×100 mg capsules) (fixed dose) once daily (QD) orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received placebo based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kilogram [kg] and Baseline platelet count >=150,000 per microliter [µL]) or 200 mg (2×100 mg capsules for participants with a baseline body weight <77 kg or baseline platelet count <150,000 per µL).

Reporting group title	Niraparib

Reporting group description:

Participants received niraparib 300 mg (3×100 mg capsules) (fixed dose) QD orally beginning on Day 1 of every cycle (each cycle of 28-days) in a double-blind fashion until a modified starting dose regimen was implemented in protocol amendment. After the protocol amendment, participants received niraparib based upon the participant's Baseline body weight or Baseline platelet count (individualized dose): 300 mg (3×100 mg capsules for participants with a Baseline body weight >=77 kg and Baseline platelet count >=150,000 per µL) or 200 mg (2×100 mg capsules for participants with a baseline body weight <77 kg or baseline platelet count <150,000 per µL).

Serious adverse events	Placebo	Niraparib	
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 244 (13.11%)	156 / 484 (32.23%)	
number of deaths (all causes)	31	48	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to breast			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Fasting			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonitis			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary embolism			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			

Device occlusion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 244 (0.00%)	20 / 484 (4.13%)	
occurrences causally related to treatment / all	0 / 0	25 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Overdose			
subjects affected / exposed	3 / 244 (1.23%)	8 / 484 (1.65%)	
occurrences causally related to treatment / all	4 / 4	4 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative hernia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 244 (0.00%)	27 / 484 (5.58%)	
occurrences causally related to treatment / all	0 / 0	27 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 244 (0.00%)	6 / 484 (1.24%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 244 (0.00%)	59 / 484 (12.19%)	
occurrences causally related to treatment / all	0 / 0	65 / 65	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal fat apron			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain lower			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 244 (0.41%)	5 / 484 (1.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Large intestinal obstruction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	5 / 244 (2.05%)	14 / 484 (2.89%)	
occurrences causally related to treatment / all	1 / 5	2 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureteric stenosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lung infection			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin bacterial infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Niraparib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	223 / 244 (91.39%)	478 / 484 (98.76%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Basal cell carcinoma			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Benign breast neoplasm			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Benign neoplasm of skin			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Cancer pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Invasive breast carcinoma			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Lipoma			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	3	2	
Seborrhoeic keratosis			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Skin papilloma			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vaginal neoplasm			

subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Embolism			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	2 / 244 (0.82%)	3 / 484 (0.62%)	
occurrences (all)	3	3	
Haematoma			
subjects affected / exposed	0 / 244 (0.00%)	7 / 484 (1.45%)	
occurrences (all)	0	7	
Hyperaemia			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Hot flush			
subjects affected / exposed	20 / 244 (8.20%)	54 / 484 (11.16%)	
occurrences (all)	20	64	
Hypertension			
subjects affected / exposed	17 / 244 (6.97%)	81 / 484 (16.74%)	
occurrences (all)	28	142	
Hypotension			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Lymphocele			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Lymphoedema			
subjects affected / exposed	3 / 244 (1.23%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Orthostatic hypotension			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	

Peripheral ischaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Pallor			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Phlebitis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Varicose vein			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Thrombosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Astringent therapy			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adhesion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	31 / 244 (12.70%)	78 / 484 (16.12%)	
occurrences (all)	47	138	
Axillary pain			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Catheter site bruise			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Catheter site haematoma			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Catheter site pain			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Catheter site rash			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Catheter site vesicles			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	3 / 244 (1.23%)	5 / 484 (1.03%)	
occurrences (all)	3	5	
Chest pain			
subjects affected / exposed	4 / 244 (1.64%)	3 / 484 (0.62%)	
occurrences (all)	4	4	
Chills			
subjects affected / exposed	3 / 244 (1.23%)	6 / 484 (1.24%)	
occurrences (all)	3	7	
Cyst			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Discomfort			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	4	
Early satiety			
subjects affected / exposed	2 / 244 (0.82%)	4 / 484 (0.83%)	
occurrences (all)	2	4	
Facial pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	72 / 244 (29.51%)	168 / 484 (34.71%)	
occurrences (all)	101	242	
Feeling abnormal			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Feeling hot			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Gait disturbance			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
General physical health deterioration			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Generalised oedema			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Hernia			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Hernia pain			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Induration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	11 / 244 (4.51%)	15 / 484 (3.10%)	
occurrences (all)	12	22	
Injection site reaction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Local swelling			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 244 (0.00%)	7 / 484 (1.45%)	
occurrences (all)	0	7	
Mass			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Mucosal dryness			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	6 / 244 (2.46%)	23 / 484 (4.75%)	
occurrences (all)	10	29	
Non-cardiac chest pain			
subjects affected / exposed	2 / 244 (0.82%)	13 / 484 (2.69%)	
occurrences (all)	2	15	
Oedema peripheral			
subjects affected / exposed	11 / 244 (4.51%)	30 / 484 (6.20%)	
occurrences (all)	19	35	
Pain			
subjects affected / exposed	6 / 244 (2.46%)	16 / 484 (3.31%)	
occurrences (all)	6	17	
Peripheral swelling			
subjects affected / exposed	4 / 244 (1.64%)	6 / 484 (1.24%)	
occurrences (all)	4	6	
Pyrexia			
subjects affected / exposed	15 / 244 (6.15%)	41 / 484 (8.47%)	
occurrences (all)	17	47	
Secretion discharge			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Sensation of foreign body			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Suprapubic pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Swelling			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Ulcer			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Unevaluable event			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Vessel puncture site bruise			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vessel puncture site haematoma			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Contrast media reaction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Seasonal allergy			
subjects affected / exposed	5 / 244 (2.05%)	3 / 484 (0.62%)	
occurrences (all)	5	3	
Reproductive system and breast disorders			
Atrophic vulvovaginitis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Breast calcifications			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Breast discharge			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Breast pain			

subjects affected / exposed	3 / 244 (1.23%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Breast tenderness			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	4	
Coital bleeding			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Dyspareunia			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Female genital tract fistula			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Genital paraesthesia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Genital swelling			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Menopausal symptoms			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Pelvic pain			
subjects affected / exposed	6 / 244 (2.46%)	8 / 484 (1.65%)	
occurrences (all)	7	8	
Metrorrhagia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Perineal pain			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Uterine polyp			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vaginal discharge			

subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	2	6	
Vaginal haemorrhage			
subjects affected / exposed	3 / 244 (1.23%)	3 / 484 (0.62%)	
occurrences (all)	3	3	
Vaginal mucosal blistering			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vaginal prolapse			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Vulvovaginal dryness			
subjects affected / exposed	6 / 244 (2.46%)	7 / 484 (1.45%)	
occurrences (all)	6	12	
Vulvovaginal pain			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Vulvovaginal pruritus			
subjects affected / exposed	4 / 244 (1.64%)	1 / 484 (0.21%)	
occurrences (all)	4	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Atelectasis			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Cough			

subjects affected / exposed	35 / 244 (14.34%)	74 / 484 (15.29%)	
occurrences (all)	45	92	
Dry throat			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Dysphonia			
subjects affected / exposed	2 / 244 (0.82%)	4 / 484 (0.83%)	
occurrences (all)	2	4	
Dyspnoea			
subjects affected / exposed	30 / 244 (12.30%)	88 / 484 (18.18%)	
occurrences (all)	33	129	
Dyspnoea at rest			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Dyspnoea exertional			
subjects affected / exposed	1 / 244 (0.41%)	17 / 484 (3.51%)	
occurrences (all)	1	18	
Epistaxis			
subjects affected / exposed	3 / 244 (1.23%)	23 / 484 (4.75%)	
occurrences (all)	6	24	
Hiccups			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Hydrothorax			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hypoxia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Interstitial lung disease			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	9 / 244 (3.69%)	21 / 484 (4.34%)	
occurrences (all)	12	28	
Nasal discomfort			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nasal dryness			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nasal pruritus			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal discomfort			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	18 / 244 (7.38%)	22 / 484 (4.55%)	
occurrences (all)	19	24	
Painful respiration			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Paranasal sinus discomfort			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	2	3	
Pleuritic pain			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	2	4	
Pneumonia aspiration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	3 / 244 (1.23%)	14 / 484 (2.89%)	
occurrences (all)	3	16	
Pulmonary embolism			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Respiratory disorder			

subjects affected / exposed	2 / 244 (0.82%)	3 / 484 (0.62%)	
occurrences (all)	3	3	
Respiratory tract congestion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	2 / 244 (0.82%)	6 / 484 (1.24%)	
occurrences (all)	2	7	
Rhinorrhoea			
subjects affected / exposed	3 / 244 (1.23%)	9 / 484 (1.86%)	
occurrences (all)	3	9	
Rhonchi			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	3 / 244 (1.23%)	2 / 484 (0.41%)	
occurrences (all)	4	3	
Sinus pain			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Tonsillar disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	3	
Wheezing			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Agitation				
subjects affected / exposed	1 / 244 (0.41%)	8 / 484 (1.65%)		
occurrences (all)	1	11		
Anxiety				
subjects affected / exposed	19 / 244 (7.79%)	43 / 484 (8.88%)		
occurrences (all)	24	53		
Confusional state				
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)		
occurrences (all)	0	3		
Depressed mood				
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)		
occurrences (all)	2	2		
Depression				
subjects affected / exposed	10 / 244 (4.10%)	26 / 484 (5.37%)		
occurrences (all)	14	28		
Dysphoria				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Emotional disorder				
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)		
occurrences (all)	0	3		
Genito-pelvic pain/penetration disorder				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Hallucination				
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)		
occurrences (all)	0	2		
Hallucination, olfactory				
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)		
occurrences (all)	1	0		
Initial insomnia				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Insomnia				

subjects affected / exposed	35 / 244 (14.34%)	119 / 484 (24.59%)	
occurrences (all)	37	162	
Irritability			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Libido decreased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Libido increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Mania			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Mood swings			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nervousness			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Nightmare			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Panic attack			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Psychotic disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Sleep disorder			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	4	
Stress			

subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Suicidal ideation			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Investigations			
Alanine aminotransferase			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Alanine aminotransferase increased			
subjects affected / exposed	15 / 244 (6.15%)	42 / 484 (8.68%)	
occurrences (all)	21	67	
Amylase increased			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Aspartate aminotransferase			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	2	
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 244 (4.10%)	43 / 484 (8.88%)	
occurrences (all)	16	78	
Bilirubin conjugated increased			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 244 (2.46%)	42 / 484 (8.68%)	
occurrences (all)	8	66	
Blood bilirubin increased			
subjects affected / exposed	0 / 244 (0.00%)	7 / 484 (1.45%)	
occurrences (all)	0	13	
Blood calcium increased			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blood chloride increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blood cholesterol increased			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	4	
Blood creatine increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	10 / 244 (4.10%)	55 / 484 (11.36%)	
occurrences (all)	12	96	
Blood glucose decreased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blood glucose increased			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	6	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Blood magnesium decreased			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Blood potassium increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	0 / 244 (0.00%)	5 / 484 (1.03%)	
occurrences (all)	0	5	
Blood sodium decreased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	

Blood urea increased				
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)		
occurrences (all)	3	4		
Bone density decreased				
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)		
occurrences (all)	1	0		
Carbohydrate antigen 125 increased				
subjects affected / exposed	10 / 244 (4.10%)	7 / 484 (1.45%)		
occurrences (all)	11	7		
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Eosinophil count decreased				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Gamma-glutamyltransferase increased				
subjects affected / exposed	2 / 244 (0.82%)	11 / 484 (2.27%)		
occurrences (all)	2	21		
Haematocrit decreased				
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)		
occurrences (all)	0	2		
Haemoglobin decreased				
subjects affected / exposed	0 / 244 (0.00%)	5 / 484 (1.03%)		
occurrences (all)	0	7		
Heart rate increased				
subjects affected / exposed	0 / 244 (0.00%)	9 / 484 (1.86%)		
occurrences (all)	0	10		
Hepatic enzyme increased				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Intraocular pressure increased				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Lipase increased				

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Lymphocyte count decreased			
subjects affected / exposed	3 / 244 (1.23%)	25 / 484 (5.17%)	
occurrences (all)	4	43	
Mean cell volume increased			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Monocyte count decreased			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Monocyte count increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	5 / 244 (2.05%)	82 / 484 (16.94%)	
occurrences (all)	10	207	
Neutrophil count increased			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Platelet count decreased			
subjects affected / exposed	3 / 244 (1.23%)	129 / 484 (26.65%)	
occurrences (all)	4	338	
Platelet count increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Protein total decreased			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Red blood cell count decreased			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Sputum abnormal			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vitamin D decreased			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	4 / 244 (1.64%)	20 / 484 (4.13%)	
occurrences (all)	6	27	
Weight increased			
subjects affected / exposed	19 / 244 (7.79%)	17 / 484 (3.51%)	
occurrences (all)	30	24	
White blood cell count decreased			
subjects affected / exposed	8 / 244 (3.28%)	74 / 484 (15.29%)	
occurrences (all)	16	205	
White blood cell count increased			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Animal bite			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Bone contusion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Chest injury			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Compression fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Contusion			

subjects affected / exposed	3 / 244 (1.23%)	22 / 484 (4.55%)	
occurrences (all)	5	29	
Fall			
subjects affected / exposed	2 / 244 (0.82%)	12 / 484 (2.48%)	
occurrences (all)	2	14	
Foot fracture			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Head injury			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Humerus fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Incision site pain			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Incision site swelling			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Incisional hernia			
subjects affected / exposed	3 / 244 (1.23%)	0 / 484 (0.00%)	
occurrences (all)	3	0	
Joint dislocation			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Laceration			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Ligament sprain			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Mallet finger			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Meniscus injury			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Muscle injury			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Muscle rupture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Post-traumatic pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Postoperative hernia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Postoperative ileus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	3 / 244 (1.23%)	6 / 484 (1.24%)	
occurrences (all)	4	6	
Procedural site reaction			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Radius fracture			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Rib fracture			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Scar			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Spinal compression fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Stoma complication			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Stoma site discharge			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Stoma site haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Stoma site inflammation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Sunburn			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Tooth fracture			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	3	
Upper limb fracture			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Vaccination complication			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vascular access malfunction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Wound			

subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Wound complication			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Wound evisceration			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Wrist fracture			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Atrial fibrillation			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Cardiac failure			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Conduction disorder			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Coronary artery disease			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Metabolic cardiomyopathy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	5 / 244 (2.05%)	39 / 484 (8.06%)	
occurrences (all)	6	45	
Sinus tachycardia			
subjects affected / exposed	3 / 244 (1.23%)	12 / 484 (2.48%)	
occurrences (all)	5	17	

Tachyarrhythmia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	6 / 244 (2.46%)	25 / 484 (5.17%)	
occurrences (all)	6	28	
Ventricular extrasystoles			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Aphasia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Aphonia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Aura			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Balance disorder			
subjects affected / exposed	0 / 244 (0.00%)	6 / 484 (1.24%)	
occurrences (all)	0	6	
Burning sensation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Carpal tunnel syndrome			
subjects affected / exposed	3 / 244 (1.23%)	3 / 484 (0.62%)	
occurrences (all)	5	3	
Cognitive disorder			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Disturbance in attention			

subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	4	
Dizziness			
subjects affected / exposed	26 / 244 (10.66%)	71 / 484 (14.67%)	
occurrences (all)	30	96	
Dizziness postural			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Dysaesthesia			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	2	
Dysgeusia			
subjects affected / exposed	10 / 244 (4.10%)	25 / 484 (5.17%)	
occurrences (all)	13	34	
Dyskinesia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Facial nerve disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	36 / 244 (14.75%)	126 / 484 (26.03%)	
occurrences (all)	46	190	
Hemiparesis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Hypoaesthesia			
subjects affected / exposed	6 / 244 (2.46%)	8 / 484 (1.65%)	
occurrences (all)	6	12	
Loss of consciousness			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Memory impairment			
subjects affected / exposed	5 / 244 (2.05%)	7 / 484 (1.45%)	
occurrences (all)	5	7	
Mental impairment			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	3 / 244 (1.23%)	4 / 484 (0.83%)	
occurrences (all)	4	5	
Motor dysfunction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	3	
Neuropathy peripheral			
subjects affected / exposed	15 / 244 (6.15%)	31 / 484 (6.40%)	
occurrences (all)	18	38	
Neurotoxicity			
subjects affected / exposed	3 / 244 (1.23%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Paraesthesia			
subjects affected / exposed	8 / 244 (3.28%)	11 / 484 (2.27%)	
occurrences (all)	9	20	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Peripheral sensory neuropathy			
subjects affected / exposed	8 / 244 (3.28%)	18 / 484 (3.72%)	
occurrences (all)	10	21	
Polyneuropathy			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Presyncope			
subjects affected / exposed	3 / 244 (1.23%)	2 / 484 (0.41%)	
occurrences (all)	3	3	
Radiculopathy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Restless legs syndrome			

subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	4	
Sciatica			
subjects affected / exposed	3 / 244 (1.23%)	9 / 484 (1.86%)	
occurrences (all)	4	10	
Seizure			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Sinus headache			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Speech disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tension headache			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	1 / 244 (0.41%)	5 / 484 (1.03%)	
occurrences (all)	1	6	
Transient global amnesia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Transient ischaemic attack			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 244 (0.00%)	7 / 484 (1.45%)	
occurrences (all)	0	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	43 / 244 (17.62%)	306 / 484 (63.22%)	
occurrences (all)	83	921	

Anaemia macrocytic			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Febrile neutropenia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Haemorrhagic disorder			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	13 / 244 (5.33%)	57 / 484 (11.78%)	
occurrences (all)	27	145	
Lymphadenitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Lymphopenia			
subjects affected / exposed	0 / 244 (0.00%)	12 / 484 (2.48%)	
occurrences (all)	0	40	
Macrocytosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	16 / 244 (6.56%)	126 / 484 (26.03%)	
occurrences (all)	32	366	

Thrombocytopenia			
subjects affected / exposed	9 / 244 (3.69%)	210 / 484 (43.39%)	
occurrences (all)	12	549	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Deafness			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Ear congestion			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Ear discomfort			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Ear haemorrhage			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	4 / 244 (1.64%)	6 / 484 (1.24%)	
occurrences (all)	4	6	
Ear pruritus			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Excessive cerumen production			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
External ear pain			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Meniere's disease			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Motion sickness			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Paraesthesia ear			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Tinnitus			
subjects affected / exposed	4 / 244 (1.64%)	11 / 484 (2.27%)	
occurrences (all)	6	11	
Vertigo			
subjects affected / exposed	6 / 244 (2.46%)	13 / 484 (2.69%)	
occurrences (all)	7	13	
Vertigo positional			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vestibular disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blepharospasm			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Cataract			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Cataract nuclear			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Conjunctival haemorrhage			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	

Conjunctivitis allergic			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	3	
Diplopia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	1 / 244 (0.41%)	11 / 484 (2.27%)	
occurrences (all)	1	12	
Eye disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Eye haemorrhage			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Eye oedema			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	5	
Eye swelling			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Eyelid oedema			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Eyelid sensory disorder			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Hypermetropia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	2	

Myopia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Ocular discomfort			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Ocular hyperaemia			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	5	
Photophobia			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Photopsia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Retinal exudates			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Retinal haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Scleral disorder			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	2 / 244 (0.82%)	5 / 484 (1.03%)	
occurrences (all)	2	5	
Visual acuity reduced			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Visual impairment			
subjects affected / exposed	1 / 244 (0.41%)	5 / 484 (1.03%)	
occurrences (all)	1	5	
Vitreous floaters			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	11 / 244 (4.51%)	15 / 484 (3.10%)	
occurrences (all)	11	19	
Abdominal distension			
subjects affected / exposed	30 / 244 (12.30%)	32 / 484 (6.61%)	
occurrences (all)	36	36	
Abdominal hernia			
subjects affected / exposed	2 / 244 (0.82%)	4 / 484 (0.83%)	
occurrences (all)	2	5	
Abdominal mass			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	74 / 244 (30.33%)	105 / 484 (21.69%)	
occurrences (all)	102	146	
Abdominal pain lower			
subjects affected / exposed	13 / 244 (5.33%)	15 / 484 (3.10%)	
occurrences (all)	17	16	
Abdominal pain upper			
subjects affected / exposed	21 / 244 (8.61%)	41 / 484 (8.47%)	
occurrences (all)	26	59	
Abdominal tenderness			
subjects affected / exposed	2 / 244 (0.82%)	4 / 484 (0.83%)	
occurrences (all)	2	6	
Abnormal faeces			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Aerophagia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Anal fissure			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Anal haemorrhage			

subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Anal incontinence			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Anal pruritus			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Anorectal discomfort			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Aphthous ulcer			
subjects affected / exposed	1 / 244 (0.41%)	5 / 484 (1.03%)	
occurrences (all)	1	5	
Ascites			
subjects affected / exposed	8 / 244 (3.28%)	3 / 484 (0.62%)	
occurrences (all)	8	3	
Cheilitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Chronic gastritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Coeliac disease			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	46 / 244 (18.85%)	189 / 484 (39.05%)	
occurrences (all)	52	262	
Defaecation urgency			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Dental caries			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Diaphragmatic hernia			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	55 / 244 (22.54%)	91 / 484 (18.80%)	
occurrences (all)	82	132	
Diverticulum intestinal			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Dry mouth			
subjects affected / exposed	6 / 244 (2.46%)	40 / 484 (8.26%)	
occurrences (all)	8	46	
Dyspepsia			
subjects affected / exposed	14 / 244 (5.74%)	34 / 484 (7.02%)	
occurrences (all)	16	43	
Dysphagia			
subjects affected / exposed	1 / 244 (0.41%)	6 / 484 (1.24%)	
occurrences (all)	1	10	
Epigastric discomfort			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Eructation			
subjects affected / exposed	3 / 244 (1.23%)	3 / 484 (0.62%)	
occurrences (all)	3	3	
Faecaloma			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Faeces discoloured			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	3	
Faeces soft			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	3	
Flatulence			
subjects affected / exposed	7 / 244 (2.87%)	17 / 484 (3.51%)	
occurrences (all)	12	20	
Frequent bowel movements			

subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Gastric disorder			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Gastritis			
subjects affected / exposed	2 / 244 (0.82%)	5 / 484 (1.03%)	
occurrences (all)	2	5	
Gastritis erosive			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Gastrointestinal disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Gastrointestinal motility disorder			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Gastrointestinal pain			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	7 / 244 (2.87%)	25 / 484 (5.17%)	
occurrences (all)	8	28	
Gingival bleeding			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Gingival pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Glossitis			

subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Glossodynia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Haematochezia			
subjects affected / exposed	3 / 244 (1.23%)	3 / 484 (0.62%)	
occurrences (all)	5	3	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	4 / 244 (1.64%)	5 / 484 (1.03%)	
occurrences (all)	4	6	
Hiatus hernia			
subjects affected / exposed	2 / 244 (0.82%)	4 / 484 (0.83%)	
occurrences (all)	2	4	
Intestinal mass			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Intestinal obstruction			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Large intestine polyp			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Lip blister			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Lip disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Lip swelling			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Melaena			

subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Mouth haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Mouth ulceration			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	5	
Nausea			
subjects affected / exposed	67 / 244 (27.46%)	278 / 484 (57.44%)	
occurrences (all)	100	448	
Noninfective gingivitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Odynophagia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Oesophagitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Oral contusion			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Oral dysaesthesia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Oral mucosal blistering			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	3	
Oral mucosal discolouration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Oral pain			
subjects affected / exposed	3 / 244 (1.23%)	7 / 484 (1.45%)	
occurrences (all)	3	9	
Pancreatic disorder			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Pancreatitis chronic			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Paraesthesia oral			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Proctalgia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Rectal discharge			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Rectal haemorrhage			
subjects affected / exposed	3 / 244 (1.23%)	5 / 484 (1.03%)	
occurrences (all)	3	7	
Rectal tenesmus			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Regurgitation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Retching			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Salivary duct stenosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Salivary gland calculus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Salivary hypersecretion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Small intestinal obstruction			

subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Stomatitis			
subjects affected / exposed	4 / 244 (1.64%)	16 / 484 (3.31%)	
occurrences (all)	7	18	
Swollen tongue			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Tongue coated			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Tooth disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tooth impacted			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 244 (0.00%)	6 / 484 (1.24%)	
occurrences (all)	0	6	
Umbilical hernia			
subjects affected / exposed	3 / 244 (1.23%)	3 / 484 (0.62%)	
occurrences (all)	3	3	
Vomiting			
subjects affected / exposed	28 / 244 (11.48%)	108 / 484 (22.31%)	
occurrences (all)	34	153	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Biliary dilatation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hepatic pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	

Hepatic steatosis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Hepatitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hepatitis toxic			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	4	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	2	8	
Hypertransaminasaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Liver disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Actinic keratosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	5 / 244 (2.05%)	7 / 484 (1.45%)	
occurrences (all)	5	7	
Angioedema			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Blood blister			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Dermal cyst			

subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Dermatitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	3	
Dermatitis acneiform			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Dermatitis contact			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	4	
Drug eruption			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	11 / 244 (4.51%)	19 / 484 (3.93%)	
occurrences (all)	12	21	
Ecchymosis			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	4	
Eczema			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	5	2	
Erythema			
subjects affected / exposed	3 / 244 (1.23%)	6 / 484 (1.24%)	
occurrences (all)	3	9	
Erythema dyschromicum perstans			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Erythema multiforme			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Hair texture abnormal			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Hirsutism			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Hyperhidrosis			
subjects affected / exposed	4 / 244 (1.64%)	8 / 484 (1.65%)	
occurrences (all)	4	8	
Hyperkeratosis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Hypertrichosis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Ingrowing nail			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Ingrown hair			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Macule			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Madarosis			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	3	
Nail discolouration			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Nail disorder			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Nail growth abnormal			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nail ridging			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Night sweats				
subjects affected / exposed	3 / 244 (1.23%)	5 / 484 (1.03%)		
occurrences (all)	4	5		
Onychoclasis				
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)		
occurrences (all)	2	1		
Onychomadesis				
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)		
occurrences (all)	1	0		
Pain of skin				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)		
occurrences (all)	1	2		
Papule				
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)		
occurrences (all)	0	1		
Petechiae				
subjects affected / exposed	0 / 244 (0.00%)	28 / 484 (5.79%)		
occurrences (all)	0	29		
Photosensitivity reaction				
subjects affected / exposed	2 / 244 (0.82%)	29 / 484 (5.99%)		
occurrences (all)	2	35		
Pityriasis				
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)		
occurrences (all)	4	0		
Pruritus				
subjects affected / exposed	19 / 244 (7.79%)	13 / 484 (2.69%)		
occurrences (all)	21	18		
Pruritus generalised				
subjects affected / exposed	5 / 244 (2.05%)	4 / 484 (0.83%)		
occurrences (all)	5	4		

Psoriasis			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Purpura			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Rash			
subjects affected / exposed	8 / 244 (3.28%)	23 / 484 (4.75%)	
occurrences (all)	12	29	
Rash generalised			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Rash macular			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Rash maculo-papular			
subjects affected / exposed	8 / 244 (3.28%)	12 / 484 (2.48%)	
occurrences (all)	8	14	
Rash pruritic			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Rosacea			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Scar pain			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Sebaceous gland disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Skin discolouration			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Skin disorder			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	

Skin exfoliation			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Skin fissures			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Skin irritation			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Skin hyperpigmentation			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Skin reaction			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Skin ulcer			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Solar dermatitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Swelling face			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Solar lentigo			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Urticaria			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Azotaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Bladder discomfort			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Bladder pain			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Bladder spasm			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Chronic kidney disease			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Cystitis interstitial			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Cystitis noninfective			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	10 / 244 (4.10%)	21 / 484 (4.34%)	
occurrences (all)	11	22	
Haematuria			
subjects affected / exposed	6 / 244 (2.46%)	5 / 484 (1.03%)	
occurrences (all)	6	6	
Leukocyturia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Micturition disorder			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	3	
Micturition urgency			

subjects affected / exposed	4 / 244 (1.64%)	3 / 484 (0.62%)	
occurrences (all)	4	3	
Nephritis			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Nephropathy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nocturia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	5 / 244 (2.05%)	11 / 484 (2.27%)	
occurrences (all)	5	11	
Polyuria			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Proteinuria			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Renal colic			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Renal failure			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Renal pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Urethral pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Urinary retention			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Urinary tract obstruction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Urinary tract pain			
subjects affected / exposed	1 / 244 (0.41%)	4 / 484 (0.83%)	
occurrences (all)	1	4	
Urine odour abnormal			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hyperthyroidism			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Hypothyroidism			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Thyroid cyst			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Thyroid mass			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	47 / 244 (19.26%)	85 / 484 (17.56%)	
occurrences (all)	77	116	
Arthritis			
subjects affected / exposed	4 / 244 (1.64%)	6 / 484 (1.24%)	
occurrences (all)	6	6	
Arthropathy			

subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	24 / 244 (9.84%)	64 / 484 (13.22%)	
occurrences (all)	29	84	
Bone disorder			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Bone lesion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	4 / 244 (1.64%)	2 / 484 (0.41%)	
occurrences (all)	6	2	
Bone swelling			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Bursitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Costochondritis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Exostosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Extremity contracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Flank pain			
subjects affected / exposed	4 / 244 (1.64%)	7 / 484 (1.45%)	
occurrences (all)	5	8	
Gouty arthritis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Groin pain			

subjects affected / exposed	3 / 244 (1.23%)	5 / 484 (1.03%)	
occurrences (all)	3	5	
Haemarthrosis			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Hypercreatinaemia			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Joint effusion			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Joint instability			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Joint range of motion decreased			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Joint stiffness			
subjects affected / exposed	4 / 244 (1.64%)	4 / 484 (0.83%)	
occurrences (all)	7	4	
Joint swelling			
subjects affected / exposed	0 / 244 (0.00%)	7 / 484 (1.45%)	
occurrences (all)	0	9	
Limb discomfort			
subjects affected / exposed	3 / 244 (1.23%)	1 / 484 (0.21%)	
occurrences (all)	3	1	
Muscle contracture			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Muscle fatigue			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Muscle spasms			

subjects affected / exposed	14 / 244 (5.74%)	19 / 484 (3.93%)	
occurrences (all)	25	24	
Muscle tightness			
subjects affected / exposed	2 / 244 (0.82%)	1 / 484 (0.21%)	
occurrences (all)	2	1	
Muscular weakness			
subjects affected / exposed	3 / 244 (1.23%)	12 / 484 (2.48%)	
occurrences (all)	3	15	
Musculoskeletal chest pain			
subjects affected / exposed	9 / 244 (3.69%)	12 / 484 (2.48%)	
occurrences (all)	10	17	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Musculoskeletal disorder			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	8 / 244 (3.28%)	12 / 484 (2.48%)	
occurrences (all)	11	15	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 244 (0.41%)	7 / 484 (1.45%)	
occurrences (all)	4	8	
Myalgia			
subjects affected / exposed	13 / 244 (5.33%)	36 / 484 (7.44%)	
occurrences (all)	18	49	
Myalgia intercostal			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	7 / 244 (2.87%)	12 / 484 (2.48%)	
occurrences (all)	9	13	
Osteoarthritis			
subjects affected / exposed	2 / 244 (0.82%)	8 / 484 (1.65%)	
occurrences (all)	2	10	
Osteochondrosis			

subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Osteonecrosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Osteopenia			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Osteoporosis			
subjects affected / exposed	1 / 244 (0.41%)	14 / 484 (2.89%)	
occurrences (all)	1	15	
Pain in extremity			
subjects affected / exposed	16 / 244 (6.56%)	38 / 484 (7.85%)	
occurrences (all)	20	53	
Pain in jaw			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Periarthritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Plantar fasciitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Psoriatic arthropathy			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Rheumatoid arthritis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Rotator cuff syndrome			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Sjogren's syndrome			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Scleroderma			

subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Soft tissue disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Spinal osteoarthritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Spondylolisthesis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Tendon pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tenosynovitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	2 / 244 (0.82%)	3 / 484 (0.62%)	
occurrences (all)	2	3	
Tenosynovitis stenosans			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Trigger finger			
subjects affected / exposed	3 / 244 (1.23%)	1 / 484 (0.21%)	
occurrences (all)	4	1	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	

Acute sinusitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Anal abscess			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Angular cheilitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Arthritis infective			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 244 (0.41%)	12 / 484 (2.48%)	
occurrences (all)	1	13	
Candida infection			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Catheter site cellulitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	3	2	
Clostridium difficile colitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 244 (0.41%)	5 / 484 (1.03%)	
occurrences (all)	1	7	
Cystitis			
subjects affected / exposed	4 / 244 (1.64%)	6 / 484 (1.24%)	
occurrences (all)	4	6	
Device related infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	

Diverticulitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Eye infection			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Folliculitis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Fungal infection			
subjects affected / exposed	4 / 244 (1.64%)	0 / 484 (0.00%)	
occurrences (all)	5	0	
Fungal skin infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Furuncle			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Gastric infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 244 (0.41%)	3 / 484 (0.62%)	
occurrences (all)	1	3	
Gastroenteritis viral			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	
Gastrointestinal candidiasis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Genital herpes			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	2	

Gingivitis			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	3	2	
Helicobacter gastritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	4 / 244 (1.64%)	5 / 484 (1.03%)	
occurrences (all)	4	8	
Hordeolum			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	5 / 244 (2.05%)	6 / 484 (1.24%)	
occurrences (all)	5	6	
Laryngitis			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Localised infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Lung infection			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	
Lymphangitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Mastitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Medical device site infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	

Mucosal infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Nail infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Onychomycosis			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Oral fungal infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	3 / 244 (1.23%)	7 / 484 (1.45%)	
occurrences (all)	4	10	
Oral infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Otitis externa			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Paronychia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Pharyngitis			
subjects affected / exposed	0 / 244 (0.00%)	5 / 484 (1.03%)	
occurrences (all)	0	6	

Pneumonia			
subjects affected / exposed	2 / 244 (0.82%)	8 / 484 (1.65%)	
occurrences (all)	2	9	
Pyelonephritis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	2 / 244 (0.82%)	3 / 484 (0.62%)	
occurrences (all)	2	3	
Respiratory tract infection viral			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	2 / 244 (0.82%)	9 / 484 (1.86%)	
occurrences (all)	2	10	
Sepsis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Shigella infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Sialoadenitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	7 / 244 (2.87%)	15 / 484 (3.10%)	
occurrences (all)	7	27	
Skin candida			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Skin infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Soft tissue infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	

Tinea pedis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	0 / 244 (0.00%)	7 / 484 (1.45%)	
occurrences (all)	0	9	
Tracheitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	18 / 244 (7.38%)	28 / 484 (5.79%)	
occurrences (all)	22	31	
Urinary tract infection			
subjects affected / exposed	19 / 244 (7.79%)	44 / 484 (9.09%)	
occurrences (all)	25	48	
Vaginal infection			
subjects affected / exposed	2 / 244 (0.82%)	3 / 484 (0.62%)	
occurrences (all)	2	4	
Viral infection			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Viral upper respiratory tract infection			
subjects affected / exposed	25 / 244 (10.25%)	49 / 484 (10.12%)	
occurrences (all)	40	55	
Vulvitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	

Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Cell death			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	20 / 244 (8.20%)	92 / 484 (19.01%)	
occurrences (all)	21	112	
Dehydration			
subjects affected / exposed	1 / 244 (0.41%)	6 / 484 (1.24%)	
occurrences (all)	1	7	
Diabetes mellitus			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	3	
Glucose tolerance impaired			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Hyperalbuminaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	1 / 244 (0.41%)	9 / 484 (1.86%)	
occurrences (all)	2	14	
Hypercholesterolaemia			
subjects affected / exposed	4 / 244 (1.64%)	7 / 484 (1.45%)	
occurrences (all)	4	7	
Hypercreatininaemia			
subjects affected / exposed	0 / 244 (0.00%)	3 / 484 (0.62%)	
occurrences (all)	0	4	
Hyperglycaemia			

subjects affected / exposed	6 / 244 (2.46%)	19 / 484 (3.93%)	
occurrences (all)	8	28	
Hyperkalaemia			
subjects affected / exposed	3 / 244 (1.23%)	6 / 484 (1.24%)	
occurrences (all)	3	10	
Hypermagnesaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hypernatraemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hyperphosphataemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Hyperproteinaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	3	
Hyperuricaemia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	2	2	
Hypoalbuminaemia			
subjects affected / exposed	3 / 244 (1.23%)	8 / 484 (1.65%)	
occurrences (all)	6	13	
Hypocalcaemia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	4	
Hypoglycaemia			
subjects affected / exposed	2 / 244 (0.82%)	2 / 484 (0.41%)	
occurrences (all)	3	2	
Hypochloraemia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 484 (0.41%)	
occurrences (all)	1	2	
Hypokalaemia			

subjects affected / exposed	4 / 244 (1.64%)	25 / 484 (5.17%)	
occurrences (all)	4	37	
Hypomagnesaemia			
subjects affected / exposed	12 / 244 (4.92%)	38 / 484 (7.85%)	
occurrences (all)	18	58	
Hyponatraemia			
subjects affected / exposed	3 / 244 (1.23%)	19 / 484 (3.93%)	
occurrences (all)	4	35	
Hypophosphataemia			
subjects affected / exposed	0 / 244 (0.00%)	2 / 484 (0.41%)	
occurrences (all)	0	10	
Hypoproteinaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Increased appetite			
subjects affected / exposed	3 / 244 (1.23%)	0 / 484 (0.00%)	
occurrences (all)	3	0	
Iron deficiency			
subjects affected / exposed	2 / 244 (0.82%)	0 / 484 (0.00%)	
occurrences (all)	2	0	
Magnesium deficiency			
subjects affected / exposed	1 / 244 (0.41%)	1 / 484 (0.21%)	
occurrences (all)	1	1	
Polydipsia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 484 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 484 (0.21%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 244 (0.00%)	4 / 484 (0.83%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2016	Amendment 1: Expanded inclusion criteria to include all participants with Stage III or IV ovarian cancer following front-line platinum-based chemotherapy treatment and not limit to participants of HRD status. Outcomes for next anticancer therapy following study treatment and time to first subsequent therapy were added as secondary endpoints. The relationship between HRD status and platinum sensitivity in ovarian cancer participants who have initial response to front-line platinum therapy was added as an exploratory objective. Stratification factors were revised to add administration of neoadjuvant chemotherapy (yes or no) and HRD status to complete response (CR)/partial response (PR). Myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) were added as adverse events of special interest. Inclusion criteria were revised to indicate high-grade and predominantly serous or endometrioid ovarian cancers, to provide more specific guidance on the surgical and chemotherapy criteria. Exclusion criteria were revised to provide more specific guidance.
16 November 2017	Amendment 2: Revision of the dosing scheme to include a fixed dose option and an individualized dose option based on a participant weight and or platelet count. The sample size was revised from 330 expected participants to 468 expected participants based on a reduced median PFS. Secondary cancers (new malignancies other than MDS/AML), pneumonitis, and embryo-fetal toxicity were added as adverse events of special interest. Rules for dose modifications were clarified based on the new fixed and individualized starting dose structure.
12 February 2018	Amendment 3: The sample size was revised from 468 expected participants to 620 expected participants based on longer median PFS expected for participants with g-breast cancer susceptibility gene (gBRCA) mutations.
27 August 2019	Amendment 4: Changed TESARO European address and sponsor medical monitor; removed secondary endpoints of outcomes for next anticancer therapy following study treatment, and time to cancer antigen 125 (CA-125) progression as they were determined to have limited clinical utility; study endpoints updated to include OS as a key secondary endpoint- defined as time from randomization to date of death; Methodology was revised to reduce frequency of computed tomography (CT)/magnetic resonance imaging (MRI) from every 12 weeks (3 cycles) to every 24 weeks (6 cycles) for participants on treatment over 2 years to reduce ionizing radiation exposure for participants on study long term; Main criteria for inclusion updated to allow for additional HRD testing following randomization; Statistical Methods updated to include Additional statistical analysis information for secondary endpoint of OS; Disease background updated to include bevacizumab as a maintenance therapy in the United States (US); extended treatment window beyond three years for those participants who are continuing to derive clinical benefit of study treatment; Discontinuation of study updated to reflect the potential for collection of OS data from public sources where available if participant withdraws consent from the study; Concomitant Medications and restrictions updated to include a requirement for a participant to withdraw from study treatment if she develops a new malignancy and requires anticancer therapy for that neoplasm; Clinical Laboratory Assessments updated to include a requirement for neutrophil collection ; Pregnancy updated Language updated to reflect Sponsor standard safety data collection practices.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported