



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 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
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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, Data analyst, Carer, 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
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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 $\geq 150,000$ 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
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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 $\geq 150,000$ 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
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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 $\geq 150,000$ 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)
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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
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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
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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
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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)
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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
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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
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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
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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
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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)
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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
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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
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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]
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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
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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]
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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
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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
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Placebo
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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 $\geq 150,000$ 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
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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 $\geq 150,000$ 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 occurrences (all)	2 / 244 (0.82%) 2	0 / 484 (0.00%) 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 occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Pallor subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	2 / 484 (0.41%) 2	
Phlebitis subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	1 / 484 (0.21%) 1	
Varicose vein subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	3 / 484 (0.62%) 3	
Thrombosis subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Astringent therapy subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
General disorders and administration site conditions Adhesion subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Asthenia subjects affected / exposed occurrences (all)	31 / 244 (12.70%) 47	78 / 484 (16.12%) 138	
Axillary pain subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Catheter site bruise subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 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 occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Unevaluable event subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Vessel puncture site bruise subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Vessel puncture site haematoma subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Immune system disorders Contrast media allergy subjects affected / exposed occurrences (all)	2 / 244 (0.82%) 2	1 / 484 (0.21%) 1	
Contrast media reaction subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Hypersensitivity subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	2 / 484 (0.41%) 2	
Seasonal allergy subjects affected / exposed occurrences (all)	5 / 244 (2.05%) 5	3 / 484 (0.62%) 3	
Reproductive system and breast disorders Atrophic vulvovaginitis subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	1 / 484 (0.21%) 1	
Breast calcifications subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Breast discharge subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 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 occurrences (all)	9 / 244 (3.69%) 12	210 / 484 (43.39%) 549	
Ear and labyrinth disorders			
Cerumen impaction subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	2 / 484 (0.41%) 2	
Deafness subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Ear congestion subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Ear discomfort subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	1 / 484 (0.21%) 1	
Ear haemorrhage subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Ear pain subjects affected / exposed occurrences (all)	4 / 244 (1.64%) 4	6 / 484 (1.24%) 6	
Ear pruritus subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Excessive cerumen production subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
External ear pain subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Hypoacusis subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 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
Onychoclasia		
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 erythrodysesthesia 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 occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Metabolism and nutrition disorders			
Cachexia subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Cell death subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	0 / 484 (0.00%) 0	
Decreased appetite subjects affected / exposed occurrences (all)	20 / 244 (8.20%) 21	92 / 484 (19.01%) 112	
Dehydration subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 1	6 / 484 (1.24%) 7	
Diabetes mellitus subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	3 / 484 (0.62%) 3	
Glucose tolerance impaired subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 2	2 / 484 (0.41%) 2	
Hyperalbuminaemia subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	1 / 484 (0.21%) 1	
Hypercalcaemia subjects affected / exposed occurrences (all)	1 / 244 (0.41%) 2	9 / 484 (1.86%) 14	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	4 / 244 (1.64%) 4	7 / 484 (1.45%) 7	
Hypercreatininaemia subjects affected / exposed occurrences (all)	0 / 244 (0.00%) 0	3 / 484 (0.62%) 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