



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 |
|-----------------------|--------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

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

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 11 July 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 444 |
| From 65 to 84 years | 287 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

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

| | |
|--|---------------|
| 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 $\geq 150,000$ 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).

| | |
|------------------|-----------|
| Arm title | Niraparib |
|------------------|-----------|

Arm description:

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

| | |
|--|---------------|
| 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 |
|-----------------------|---------|

Reporting group description:

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

| | |
|-----------------------|-----------|
| Reporting group title | Niraparib |
|-----------------------|-----------|

Reporting group description:

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

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

End points

End points reporting groups

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

Primary: Progression free survival

| | |
|--|---------------------------|
| End point title | Progression free survival |
| End point description: | |
| Progression free survival was defined as the time from the date of treatment randomization to the date of first documentation of disease progression or death due to any cause in the absence of documented progression, whichever occurs first. It was assessed by the blinded independent central review (BICR). Median and 95% confidence interval (CI) are presented. Intent-to-Treat (ITT) population comprised of all participants who were randomized into the study. | |
| End point type | Primary |
| End point timeframe: | |
| Up to 34 months | |

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

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo. | |
| Comparison groups | Placebo v Niraparib |

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

Notes:

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

Secondary: Overall Survival

| | |
|--|------------------|
| End point title | Overall Survival |
| End point description: | |
| Overall survival was defined as the time from the date of randomization to the date of death by any cause. Median and 95% CI are presented for overall survival interim analysis. 99999 indicates, median and 95% CI (upper limit) could not be derived, as <50% of participants experienced the event within the treatment arm. 88888 indicates, 95% CI (upper limit) could not be derived, as <75% of participants experienced the event within the treatment arm. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 34 months | |

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

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo. | |
| Comparison groups | Placebo v Niraparib |

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

Notes:

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

Secondary: Time to first subsequent therapy (TFST)

| | |
|--|---|
| End point title | Time to first subsequent therapy (TFST) |
| End point description: | |
| Time to first subsequent therapy was defined as the time from the date of randomization to the date of the first subsequent anti-cancer therapy or death, whichever occurs first. Median and 95% CI are presented. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 34 months | |

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

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo. | |
| Comparison groups | Placebo v Niraparib |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 ^[9] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.65 |

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

Notes:

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

Secondary: Progression-Free Survival-2 (PFS2)

| | |
|---|------------------------------------|
| End point title | Progression-Free Survival-2 (PFS2) |
| End point description: | |
| PFS2 was defined as the time from the date of randomization to the date of progression on the next anti-cancer therapy following study treatment or death by any cause, whichever occurs first. Median and 95% CI are presented. 99999 indicates, median and 95% CI could not be derived, as <25% of participants experienced the event within the treatment arm. 88888 indicates, 95% CI (upper limit) could not be derived, as <75% of participants experienced the event within the treatment arm. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 34 months | |

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

Notes:

[10] - ITT Population

[11] - ITT Population

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| If hazard ratio was found to be <1 then niraparib can be considered as superior to placebo. | |
| Comparison groups | Placebo v Niraparib |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2242 ^[12] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.577 |
| upper limit | 1.139 |

Notes:

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

[17] - ITT Population

[18] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1, Pre-dose) and Up to Week 24 | |

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

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1, Pre-dose) and Up to 34 months | |

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

Notes:

[23] - ITT Population

[24] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|--|
| End point title | Change from Baseline in symptoms scale of EORTC-QLQ-OV28 |
| End point description: | |
| EORTC-QLQ-OV28 is supplement to EORTC-QLQ-C30. It includes 3 functional scales (body image, sexuality, attitude to disease/treatment) and 5 symptom scales/items (abdominal/GI symptoms, peripheral neuropathy, hormonal/menopausal symptoms, other chemotherapy side-effects, and hair loss). Symptoms scales score was calculated by averaging scores of all scale items and transforming average scores linearly ([average score minus 1] divided by 3*100). All of the symptoms scales range in score from 0 to 100. Higher score represents a higher ("worse") level of symptoms. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles). | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1, Pre-dose) and Up to 34 months | |

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

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

Notes:

[25] - ITT Population

[26] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 34 months

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

Notes:

[27] - Safety Population

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 34 months

Notes:

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

Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

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

Notes:

[30] - ITT Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Peak plasma concentration (Cmax)

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

End point description:

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

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 34 months

Notes:

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

Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

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

Notes:

[32] - ITT Population

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Number of participants with positive HRD test |
|-----------------|---|

End point description:

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

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 34 months

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

Notes:

[33] - ITT Population

[34] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

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

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

| | | | |
|---|-------------------------|--------------------------|--|
| Peripheral ischaemia subjects affected / exposed 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 | | | |

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|---|------------------|------------------|
| 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 | | |

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|--------------------------------|-----------------|--------------------|
| 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 | | |

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| 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 | | |

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| 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 | |

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|---------------------------------|------------------|--------------------|
| 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 | | | |

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| 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 | |

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| 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 |

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| 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 |

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| 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 | | | |

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| 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 | | |

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|-----------------------------|-------------------|-------------------|
| 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 | | |

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|------------------------------------|-----------------|------------------|
| 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 | |
| Hypertransaminaemia | | | |
| 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 | | | |

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|--------------------------------|------------------|------------------|
| 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 erythrodysaesthesia syndrome | | |
| subjects affected / exposed | 1 / 244 (0.41%) | 2 / 484 (0.41%) |
| occurrences (all) | 1 | 2 |
| Papule | | |
| subjects affected / exposed | 0 / 244 (0.00%) | 1 / 484 (0.21%) |
| occurrences (all) | 0 | 1 |
| Petechiae | | |
| subjects affected / exposed | 0 / 244 (0.00%) | 28 / 484 (5.79%) |
| occurrences (all) | 0 | 29 |
| Photosensitivity reaction | | |
| subjects affected / exposed | 2 / 244 (0.82%) | 29 / 484 (5.99%) |
| occurrences (all) | 2 | 35 |
| Pityriasis | | |
| subjects affected / exposed | 1 / 244 (0.41%) | 0 / 484 (0.00%) |
| occurrences (all) | 4 | 0 |
| Pruritus | | |
| subjects affected / exposed | 19 / 244 (7.79%) | 13 / 484 (2.69%) |
| occurrences (all) | 21 | 18 |
| Pruritus generalised | | |
| subjects affected / exposed | 5 / 244 (2.05%) | 4 / 484 (0.83%) |
| occurrences (all) | 5 | 4 |

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|-----------------------------|-----------------|------------------|
| 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 |

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| 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 | | | |

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|-----------------------------|------------------|------------------|
| 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 | | |

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|-----------------------------|-----------------|------------------|
| 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 | | |

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|---|-------------------|-------------------|--|
| 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 |

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|-----------------------------|-----------------|-----------------|
| 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 | | | |

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|-----------------------------|-----------------|------------------|
| 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