



Clinical trial results:

An open-label, parallel-group, randomized, multicenter study to assess the safety and efficacy of vilaprisan in subjects with uterine fibroids versus standard of care

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-004822-41 |
| Trial protocol | CZ FI PL |
| Global end of trial date | 11 July 2024 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v2 (current) |
| This version publication date | 13 July 2025 |
| First version publication date | 14 September 2023 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY1002670/16953 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03194646 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 20 May 2025 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 11 July 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety of vilaprisan in subjects with uterine fibroids in comparison to nonhormonal medical treatment in accordance with local standard of care. With the implementation of protocol amendment 10, Version 7.0 for the comprehensive safety follow up, additional focus was put on safety evaluations of the endometrium, adrenal glands, and skin.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 30 June 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Czechia: 238 |
| Country: Number of subjects enrolled | China: 73 |
| Country: Number of subjects enrolled | Finland: 9 |
| Country: Number of subjects enrolled | Hong Kong: 7 |
| Country: Number of subjects enrolled | Japan: 322 |
| Country: Number of subjects enrolled | Mexico: 72 |
| Country: Number of subjects enrolled | Norway: 19 |
| Country: Number of subjects enrolled | Poland: 114 |
| Country: Number of subjects enrolled | Russian Federation: 39 |
| Country: Number of subjects enrolled | Thailand: 13 |
| Country: Number of subjects enrolled | Türkiye: 23 |
| Country: Number of subjects enrolled | United States: 1359 |
| Country: Number of subjects enrolled | South Africa: 80 |
| Worldwide total number of subjects | 2368 |
| EEA total number of subjects | 380 |

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) | 2368 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 219 study centers in 13 countries worldwide between 30-Jun-2017 (first subject first visit) and 11-Jul-2024 (Last subject last follow-up visit).

Pre-assignment

Screening details:

Overall, 2368 subjects were screened. Of the 2368 screened subjects, 1096 (46.3%) subjects were not randomized to treatment due to screen failures. 1272 (53.7%) subjects were randomized. 1238 (52.3%) subjects received study treatment and were included in Safety analysis set.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Vilaprisan 2 mg A1 (3/1 regimen) |

Arm description:

4 treatment periods of 12 weeks, each separated by 1 bleeding episode

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vilaprisan |
| Investigational medicinal product code | BAY1002670 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

2 mg, once daily

| | |
|------------------|----------------------------------|
| Arm title | Vilaprisan 2 mg A2 (6/2 regimen) |
|------------------|----------------------------------|

Arm description:

2 treatment periods of 24 weeks, separated by 2 bleeding episodes

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vilaprisan |
| Investigational medicinal product code | BAY1002670 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

2 mg, once daily

| | |
|------------------|----------------------------------|
| Arm title | Vilaprisan 2 mg A3 (3/2 regimen) |
|------------------|----------------------------------|

Arm description:

3 treatment periods of 12 weeks, each separated by 2 bleeding episodes

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vilaprisan |
| Investigational medicinal product code | BAY1002670 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

2 mg, once daily

| | |
|---|------------------------|
| Arm title | B (Standard of care) |
| Arm description: Standard of care symptomatic nonhormonal medical treatment as determined by the investigators and/or watch and wait | |
| Arm type | Standard of care (SoC) |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1^[1] | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) |
|---|----------------------------------|----------------------------------|----------------------------------|
| Started | 349 | 347 | 177 |
| Completed | 59 | 93 | 44 |
| Not completed | 290 | 254 | 133 |
| Consent withdrawn by subject | 69 | 72 | 34 |
| Physician decision | 6 | 9 | 5 |
| Adverse event, non-fatal | 24 | 25 | 14 |
| Pregnancy | 4 | 5 | 1 |
| Site terminated by sponsor | - | - | 2 |
| Non-compliance with study drug | 3 | - | 1 |
| Study terminated by sponsor | 62 | 60 | 29 |
| Unspecified | 87 | 59 | 33 |
| Lost to follow-up | 29 | 21 | 11 |
| Missing | 1 | - | 1 |
| Lack of efficacy | 4 | 2 | 2 |
| Protocol deviation | 1 | 1 | - |

| Number of subjects in period 1^[1] | B (Standard of care) |
|---|----------------------|
| Started | 365 |
| Completed | 85 |
| Not completed | 280 |
| Consent withdrawn by subject | 131 |
| Physician decision | 4 |
| Adverse event, non-fatal | 17 |
| Pregnancy | 2 |
| Site terminated by sponsor | - |
| Non-compliance with study drug | 1 |

| | |
|-----------------------------|----|
| Study terminated by sponsor | 34 |
| Unspecified | 31 |
| Lost to follow-up | 35 |
| Missing | 12 |
| Lack of efficacy | 12 |
| Protocol deviation | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Overall, 2368 subjects were enrolled and screened. Of the 2368 screened subjects, 1096 (46.3%) subjects were not randomized to treatment due to screen failures. 1272 (53.7%) subjects were randomized, assigned to treatment and entered the treatment period.

Baseline characteristics

Reporting groups

| | |
|---|----------------------------------|
| Reporting group title | Vilaprisan 2 mg A1 (3/1 regimen) |
| Reporting group description: | |
| 4 treatment periods of 12 weeks, each separated by 1 bleeding episode | |
| Reporting group title | Vilaprisan 2 mg A2 (6/2 regimen) |
| Reporting group description: | |
| 2 treatment periods of 24 weeks, separated by 2 bleeding episodes | |
| Reporting group title | Vilaprisan 2 mg A3 (3/2 regimen) |
| Reporting group description: | |
| 3 treatment periods of 12 weeks, each separated by 2 bleeding episodes | |
| Reporting group title | B (Standard of care) |
| Reporting group description: | |
| Standard of care symptomatic nonhormonal medical treatment as determined by the investigators and/or watch and wait | |

| Reporting group values | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) |
|------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Number of subjects | 349 | 347 | 177 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|-------|-------|
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 41.7 | 41.5 | 41.8 |
| standard deviation | ± 5.9 | ± 6.0 | ± 5.9 |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 349 | 347 | 177 |
| Male | 0 | 0 | 0 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 6 | 6 | 2 |
| Asian | 120 | 123 | 63 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 96 | 87 | 41 |
| White | 124 | 125 | 70 |
| More than one race | 3 | 3 | 0 |
| Unknown or Not Reported | 0 | 3 | 1 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 26 | 33 | 15 |
| Not Hispanic or Latino | 320 | 312 | 162 |
| Unknown or Not Reported | 3 | 2 | 0 |
| Endometrial thickness | | | |

Ultrasound examinations were performed. Endometrial thickness was measured in the medio-sagittal section as double-layer in millimeters. Baseline data (Last non-missing value before reference start date) of endometrial thickness is provided in below table. Safety analysis set (SAF) was analyzed. Some data in baseline were missing. The actual analyzed number for A1: 348, A2: 344, A3: 176 and B: 363

| | | | |
|---|----------|----------|----------|
| and the total number is 1231. | | | |
| Units: Millimeters | | | |
| arithmetic mean | 8.3 | 8.3 | 8.6 |
| standard deviation | ± 3.8 | ± 4.0 | ± 3.8 |
| Baseline bone mineral density (BMD) of lumbar spine | | | |
| The baseline data of BMD measured by dual-energy X-ray absorptiometry (DEXA) scan for lumbar spine is provided in below table. SAF was analyzed. Subjects were analyzed as treated. Some data in baseline was missing. The actual number analyzed for A1: 339, A2: 338, A3: 174, B: 350 and total number is 1201. | | | |
| Units: g/cm ² | | | |
| arithmetic mean | 1.1468 | 1.1653 | 1.1560 |
| standard deviation | ± 0.1869 | ± 0.1889 | ± 0.1807 |
| Baseline bone mineral density (BMD) of hip | | | |
| The baseline data of BMD measured by dual-energy X-ray absorptiometry (DEXA) scan for hip is provided in below table. SAF was analyzed. Some data in baseline was missing. The actual number analyzed for A1: 340, A2: 337, A3: 174, B: 357 and total number is 1208. | | | |
| Units: g/cm ² | | | |
| arithmetic mean | 0.9998 | 1.0044 | 1.0063 |
| standard deviation | ± 0.1528 | ± 0.1614 | ± 0.1508 |
| Baseline bone mineral density (BMD) of femoral neck | | | |
| The baseline data of BMD measured by dual-energy X-ray absorptiometry (DEXA) scan for femoral neck is provided in below table. SAF was analyzed. Some data in baseline was missing. The actual number analyzed for A1: 340, A2: 337, A3: 174, B: 357 and total number is 1208. | | | |
| Units: g/cm ² | | | |
| arithmetic mean | 0.9050 | 0.9174 | 0.9150 |
| standard deviation | ± 0.1700 | ± 0.1808 | ± 0.1730 |

| Reporting group values | B (Standard of care) | Total | |
|------------------------|----------------------|-------|--|
| Number of subjects | 365 | 1238 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|------|--|
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 42.2 | | |
| standard deviation | ± 6.1 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 365 | 1238 | |
| Male | 0 | 0 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 3 | 17 | |
| Asian | 129 | 435 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 100 | 324 | |
| White | 132 | 451 | |
| More than one race | 0 | 6 | |
| Unknown or Not Reported | 1 | 5 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |

| | | | |
|---|----------|------|--|
| Hispanic or Latino | 35 | 109 | |
| Not Hispanic or Latino | 327 | 1121 | |
| Unknown or Not Reported | 3 | 8 | |
| Endometrial thickness | | | |
| <p>Ultrasound examinations were performed. Endometrial thickness was measured in the medio-sagittal section as double-layer in millimeters. Baseline data (Last non-missing value before reference start date) of endometrial thickness is provided in below table. Safety analysis set (SAF) was analyzed. Some data in baseline were missing. The actual analyzed number for A1: 348, A2: 344, A3: 176 and B: 363 and the total number is 1231.</p> | | | |
| Units: Millimeters | | | |
| arithmetic mean | 8.7 | | |
| standard deviation | ± 4.3 | - | |
| Baseline bone mineral density (BMD) of lumbar spine | | | |
| <p>The baseline data of BMD measured by dual-energy X-ray absorptiometry (DEXA) scan for lumbar spine is provided in below table. SAF was analyzed. Subjects were analyzed as treated. Some data in baseline was missing. The actual number analyzed for A1: 339, A2: 338, A3: 174, B: 350 and total number is 1201.</p> | | | |
| Units: g/cm ² | | | |
| arithmetic mean | 1.1532 | | |
| standard deviation | ± 0.1851 | - | |
| Baseline bone mineral density (BMD) of hip | | | |
| <p>The baseline data of BMD measured by dual-energy X-ray absorptiometry (DEXA) scan for hip is provided in below table. SAF was analyzed. Some data in baseline was missing. The actual number analyzed for A1: 340, A2: 337, A3: 174, B: 357 and total number is 1208.</p> | | | |
| Units: g/cm ² | | | |
| arithmetic mean | 0.9944 | | |
| standard deviation | ± 0.1486 | - | |
| Baseline bone mineral density (BMD) of femoral neck | | | |
| <p>The baseline data of BMD measured by dual-energy X-ray absorptiometry (DEXA) scan for femoral neck is provided in below table. SAF was analyzed. Some data in baseline was missing. The actual number analyzed for A1: 340, A2: 337, A3: 174, B: 357 and total number is 1208.</p> | | | |
| Units: g/cm ² | | | |
| arithmetic mean | 0.9021 | | |
| standard deviation | ± 0.1703 | - | |

End points

End points reporting groups

| | |
|---|----------------------------------|
| Reporting group title | Vilaprisan 2 mg A1 (3/1 regimen) |
| Reporting group description: 4 treatment periods of 12 weeks, each separated by 1 bleeding episode | |
| Reporting group title | Vilaprisan 2 mg A2 (6/2 regimen) |
| Reporting group description: 2 treatment periods of 24 weeks, separated by 2 bleeding episodes | |
| Reporting group title | Vilaprisan 2 mg A3 (3/2 regimen) |
| Reporting group description: 3 treatment periods of 12 weeks, each separated by 2 bleeding episodes | |
| Reporting group title | B (Standard of care) |
| Reporting group description: Standard of care symptomatic nonhormonal medical treatment as determined by the investigators and/or watch and wait | |
| Subject analysis set title | Full analysis set (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The FAS consisted of all randomized subjects, excluding randomized subjects who did not start Treatment Period 1 due to the study being temporarily paused (subject did not receive any study drug because of the partial clinical hold 8 [0.6%]), and included 1264 (99.4%) subjects. | |
| Subject analysis set title | Safety analysis set (SAF) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The SAF consisted of all subjects randomized to vilaprisan (VPR) treatment groups who took at least 1 dose of study drug and all 365 subjects randomized to treatment group B (SoC) and included 1238 (97.3%) subjects. | |

Primary: Percentage change in bone mineral density (BMD) of lumbar spine

| | |
|---|---|
| End point title | Percentage change in bone mineral density (BMD) of lumbar spine |
| End point description: The percentage change in BMD (measured by dual-energy X-ray absorptiometry (DEXA) scan) of lumbar spine from baseline to about one year after start of treatment (SoT) in all randomized and treated participants with measurements at those 2 time points in each treatment group. | |
| End point type | Primary |
| End point timeframe: From baseline to about 1 year after start of treatment | |

| End point values | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) | B (Standard of care) |
|--------------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 112 | 143 | 57 | 181 |
| Units: Percentage change | | | | |
| arithmetic mean (standard deviation) | -1.56 (± 2.72) | -2.04 (± 2.50) | -1.51 (± 2.28) | 0.29 (± 2.36) |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | VPR A1 - SoC |
| Comparison groups | Vilaprisan 2 mg A1 (3/1 regimen) v B (Standard of care) |
| Number of subjects included in analysis | 293 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.44 |
| upper limit | -1.26 |

| | |
|---|---|
| Statistical analysis title | VPR A2 - SoC |
| Comparison groups | Vilaprisan 2 mg A2 (6/2 regimen) v B (Standard of care) |
| Number of subjects included in analysis | 324 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.87 |
| upper limit | -1.8 |

| | |
|---|---|
| Statistical analysis title | VPR A3 - SoC |
| Comparison groups | Vilaprisan 2 mg A3 (3/2 regimen) v B (Standard of care) |
| Number of subjects included in analysis | 238 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.51 |
| upper limit | -1.1 |

Secondary: Number of bleeding days

| | |
|-----------------|-------------------------|
| End point title | Number of bleeding days |
|-----------------|-------------------------|

End point description:

Number of bleeding days were defined from Day 1 of the first treatment period until the day before a new treatment period would start again following the last treatment period for that respective treatment group. Number to be normalized by 28 days

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

End point timeframe:

Treatment phase: approximately 1 year

| End point values | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) | B (Standard of care) |
|--------------------------------------|--|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 349 | 347 | 177 | 365 |
| Units: Days | | | | |
| arithmetic mean (standard deviation) | 1.57 (± 1.99) | 1.74 (± 2.52) | 1.81 (± 1.24) | 4.72 (± 4.60) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in BMD measured at lumbar spine (other time points not mentioned as primary safety variable) and hip/femoral neck

| | |
|-----------------|---|
| End point title | Percentage change from baseline in BMD measured at lumbar spine (other time points not mentioned as primary safety variable) and hip/femoral neck |
|-----------------|---|

End point description:

This was analyzed using the same statistical methods as the primary variable. Subjects analyzed: Lumbar spine (LS) – Month (M) 6 on treatment: A1:15, A2:35, A3:8, B:8 LS - End of treatment (EoT): A1:100, A2:172, A3:67, B:161 LS - M 6 post treatment: A1:127, A2:144, A3:75, B:93 LS - M 12 post treatment: A1:7, A2:13, A3:6, B:13 LS - End of follow up (EoFUP): A1:246, A2:245, A3:125, B:113 Hip - M 6 on treatment: A1:16, A2:35, A3:8, B:8 Hip - M 12 on treatment: A1:112, A2:143, A3:56, B:182 Hip - EoT: A1:101, A2:172, A3:67, B:162 Hip - M 6 post treatment: A1:127, A2:144, A3:74, B:93 Hip - M 12 post treatment: A1:7, A2:13, A3:6, B:14 Hip - EoFUP: A1:247, A2:244, A3:125, B:114 Femoral neck (FN) - M 6 on treatment: A1:16, A2:35, A3:8, B:8 FN - M 12 on treatment: A1:112, A2:143, A3:56, B:182 FN - EoT: A1:101, A2:172, A3:67, A3:162 FN - M 6 post treatment: A1:127, A2:144, A3:74, B:93 FN - M 12 post treatment: A1:7, A2:13, A3:6, B:14 FN - EoFUP: A1:247, A2:244, A3:125,

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

End point timeframe:

Treatment phase: approximately 1 year, follow-up phase: up to 2 years

| End point values | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) | B (Standard of care) |
|--------------------------------------|--|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 349 | 347 | 177 | 365 |
| Units: Percentage change | | | | |
| arithmetic mean (standard deviation) | | | | |
| LS - M 6 on treatment | -0.18 (± 1.70) | -0.49 (± 2.74) | 0.51 (± 2.52) | -0.88 (± 2.60) |

| | | | | |
|---------------------------|----------------|----------------|----------------|----------------|
| LS - EoT | -1.48 (± 2.68) | -1.76 (± 2.64) | -1.22 (± 2.36) | 0.13 (± 2.38) |
| LS - M 6 post treatment | -0.69 (± 3.30) | -0.89 (± 2.72) | -0.57 (± 2.36) | -0.17 (± 2.76) |
| LS - M 12 post treatment | -0.10 (± 2.81) | -0.45 (± 3.61) | 0.86 (± 2.73) | 1.03 (± 6.79) |
| LS - EoFUP | -0.64 (± 4.23) | -0.28 (± 4.11) | -0.38 (± 4.26) | -0.07 (± 3.49) |
| Hip - M 6 on treatment | -1.00 (± 2.89) | -0.48 (± 2.49) | 1.54 (± 1.21) | -0.23 (± 1.81) |
| Hip - M 12 on treatment | -0.84 (± 2.19) | -0.99 (± 2.23) | -0.91 (± 2.68) | -0.03 (± 2.47) |
| Hip - EoT | -0.85 (± 2.28) | -0.91 (± 2.34) | -0.61 (± 2.63) | -0.06 (± 2.65) |
| Hip - M 6 post treatment | -0.45 (± 2.30) | -0.62 (± 2.60) | -0.54 (± 3.06) | 0.20 (± 2.72) |
| Hip - M 12 post treatment | -0.72 (± 1.95) | -0.33 (± 1.91) | 1.41 (± 2.22) | -0.23 (± 3.77) |
| Hip - EoFUP | -0.80 (± 3.06) | -0.03 (± 3.85) | -0.20 (± 3.81) | 0.08 (± 2.91) |
| FN - M 6 on treatment | -0.71 (± 2.69) | 0.66 (± 3.27) | 1.23 (± 3.08) | 0.08 (± 3.80) |
| FN - M 12 on treatment | -0.84 (± 3.42) | -0.64 (± 3.45) | -0.66 (± 3.07) | -0.01 (± 3.42) |
| FN - EoT | -1.12 (± 3.37) | -0.36 (± 3.46) | -0.42 (± 3.21) | -0.02 (± 3.47) |
| FN - M 6 post treatment | -0.87 (± 3.45) | -0.49 (± 3.52) | -0.35 (± 3.80) | -0.42 (± 3.32) |
| FN - M 12 post treatment | -0.82 (± 3.83) | -1.27 (± 3.60) | -0.65 (± 1.06) | 1.40 (± 5.19) |
| FN - EoFUP | -0.90 (± 4.41) | -0.09 (± 5.16) | -0.52 (± 5.70) | -0.34 (± 3.73) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with endometrial histology findings by endometrial biopsy main results (majority read, main diagnosis)

| | |
|---|---|
| End point title | Number of participants with endometrial histology findings by endometrial biopsy main results (majority read, main diagnosis) |
| End point description: | |
| Number of participants with endometrial histology findings, e.g. benign endometrium, presence or absence of hyperplasia or malignancy | |
| End point type | Secondary |
| End point timeframe: | |
| Treatment phase: approximately 1 year, follow-up phase: up to 2 years | |

| End point values | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) | B (Standard of care) |
|---------------------------------|--|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 349 | 347 | 177 | 365 |
| Units: Participants | | | | |
| Adequate endometrial tissue | 346 | 346 | 175 | 359 |
| Benign Endometrium | 346 | 346 | 175 | 359 |
| Hyperplasia WHO 2014, no atypia | 0 | 0 | 0 | 0 |
| Hyperplasia WHO 2014, atypia | 0 | 0 | 0 | 0 |
| Malignant Neoplasm | 0 | 0 | 0 | 0 |
| Endometrial Polyps | 6 | 8 | 4 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in endometrial thickness

| | |
|-----------------|---|
| End point title | Change from baseline in endometrial thickness |
|-----------------|---|

End point description:

Ultrasound examinations were performed. Endometrial thickness was measured in the medio-sagittal section as double-layer in millimeters. Summary statistics for change from baseline (worst measurement during baseline period) in endometrial thickness was provided in below table.

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

End point timeframe:

Treatment phase: approximately 1 year, follow-up phase: up to 2 years

| End point values | Vilaprisan 2 mg A1 (3/1 regimen) | Vilaprisan 2 mg A2 (6/2 regimen) | Vilaprisan 2 mg A3 (3/2 regimen) | B (Standard of care) |
|---|--|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 348 ^[1] | 344 ^[2] | 176 ^[3] | 363 ^[4] |
| Units: Millimeters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 10.4 (± 4.0) | 10.7 (± 4.0) | 10.9 (± 4.0) | 11.0 (± 4.4) |
| Treatment phase (change from baseline) | -0.5 (± 5.6) | -0.2 (± 5.7) | -0.9 (± 4.7) | -0.4 (± 4.5) |
| Follow up phase (change from baseline) | -0.2 (± 5.2) | -0.3 (± 5.7) | -1.1 (± 4.5) | -2.7 (± 4.6) |

Notes:

[1] - Baseline: 348 Treatment phase(change from baseline): 264 Followup phase(change from baseline): 323

[2] - Baseline: 344 Treatment phase(change from baseline): 318 Followup phase(change from baseline): 307

[3] - Baseline: 176 Treatment phase(change from baseline): 127 Followup phase(change from baseline): 163

[4] - Baseline: 363 Treatment phase(change from baseline): 316 Followup phase(change from baseline): 142

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

ABBREVIATED: For TEAEs: From the first application of study med up to 60 calendar days after end of treatment with study med (mean duration is 321 days). For Post-treatment AEs: All AEs that started from Day 61 after the end of treatment with study med

Adverse event reporting additional description:

Treatment emergent adverse events = TEAEs

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Vilaprisan 2 mg A1 (3/1 regimen) - Treatment emergent AEs |
|-----------------------|---|

Reporting group description:

4 treatment periods of 12 weeks, each separated by 1 bleeding episode (3/1 regimen)

| | |
|-----------------------|---|
| Reporting group title | Vilaprisan 2 mg A2 (6/2 regimen) - Treatment emergent AEs |
|-----------------------|---|

Reporting group description:

2 treatment periods of 24 weeks, separated by 2 bleeding episodes

| | |
|-----------------------|---|
| Reporting group title | Vilaprisan 2 mg A3 (3/2 regimen) - Treatment emergent AEs |
|-----------------------|---|

Reporting group description:

3 treatment periods of 12 weeks, each separated by 2 bleeding episodes

| | |
|-----------------------|---|
| Reporting group title | Standard of care B - Treatment emergent AEs |
|-----------------------|---|

Reporting group description:

Standard of care symptomatic nonhormonal medical treatment as determined by the investigators and/or watch and wait

| | |
|-----------------------|---|
| Reporting group title | Vilaprisan 2 mg A2 (6/2 regimen) - Post treatment AEs |
|-----------------------|---|

Reporting group description:

2 treatment periods of 24 weeks, separated by 2 bleeding episodes

| | |
|-----------------------|---|
| Reporting group title | Vilaprisan 2 mg A1 (3/1 regimen) - Post treatment AEs |
|-----------------------|---|

Reporting group description:

4 treatment periods of 12 weeks, each separated by 1 bleeding episode (3/1 regimen)

| | |
|-----------------------|---|
| Reporting group title | Vilaprisan 2 mg A3 (3/2 regimen) - Post treatment AEs |
|-----------------------|---|

Reporting group description:

3 treatment periods of 12 weeks, each separated by 2 bleeding episodes

| | |
|-----------------------|---|
| Reporting group title | Standard of care B - Post treatment AEs |
|-----------------------|---|

Reporting group description:

Standard of care symptomatic nonhormonal medical treatment as determined by the investigators and/or watch and wait

| Serious adverse events | Vilaprisan 2 mg A1 (3/1 regimen) - Treatment emergent AEs | Vilaprisan 2 mg A2 (6/2 regimen) - Treatment emergent AEs | Vilaprisan 2 mg A3 (3/2 regimen) - Treatment emergent AEs |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 349 (4.30%) | 17 / 347 (4.90%) | 6 / 177 (3.39%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from | 0 | 0 | 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acoustic neuroma | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal adenoma | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian adenoma | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phyllodes tumour | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer female | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Benign mesenteric neoplasm | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive breast carcinoma | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine myoma expulsion | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign neoplasm of adrenal gland | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Degeneration of uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Hysterectomy | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicectomy | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mastectomy | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myomectomy | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 2 / 347 (0.58%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingectomy | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hysterosalpingo-oophorectomy | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fusion surgery | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial ablation | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cyst removal | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device removal | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hysterosalpingectomy | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shoulder operation | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine dilation and curettage | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus removal | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingo-oophorectomy bilateral | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Simple mastectomy | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine artery embolisation | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal adhesiolysis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion threatened | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical cord abnormality | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Premature delivery | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Cervical cyst | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical polyp | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic adhesions | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal haematoma | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenomyosis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic discomfort | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heavy menstrual bleeding | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abnormal uterine bleeding | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic organ prolapse | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial hyperplasia with cellular atypia | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Substance abuse | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biopsy peritoneum | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Norepinephrine increased | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood pressure increased | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scan adrenal gland abnormal | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia postoperative | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic fracture | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Venous angioma of brain | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRCA1 gene mutation | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Transient ischaemic attack subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal epidural haematoma subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Central nervous system lesion subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aplastic anaemia subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency anaemia subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis ulcerative subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Primary hyperaldosteronism | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal mass | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid mass | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Synovitis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 1 / 347 (0.29%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometritis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mastitis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Periodontitis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 349 (0.00%) | 0 / 347 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 0 / 347 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Standard of care B - Treatment emergent AEs | Vilaprisan 2 mg A2 (6/2 regimen) - Post treatment AEs | Vilaprisan 2 mg A1 (3/1 regimen) - Post treatment AEs |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 365 (4.66%) | 42 / 347 (12.10%) | 54 / 349 (15.47%) |
| number of deaths (all causes) | 0 | 0 | 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acoustic neuroma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal adenoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 2 / 347 (0.58%) | 8 / 349 (2.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 6 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 2 / 349 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 3 / 365 (0.82%) | 3 / 347 (0.86%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian adenoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phyllodes tumour | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer female | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign mesenteric neoplasm | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive breast carcinoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine myoma expulsion | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign neoplasm of adrenal gland | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Degeneration of uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 2 / 349 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Thrombosis | | | |

| | | | |
|---|-----------------|------------------|------------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Hysterectomy | | | |
| subjects affected / exposed | 2 / 365 (0.55%) | 16 / 347 (4.61%) | 18 / 349 (5.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 16 | 2 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicectomy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mastectomy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myomectomy | | | |
| subjects affected / exposed | 2 / 365 (0.55%) | 5 / 347 (1.44%) | 6 / 349 (1.72%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingectomy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hysterosalpingo-oophorectomy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fusion surgery | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial ablation | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cyst removal | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device removal | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hysterosalpingectomy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 3 / 349 (0.86%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shoulder operation | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine dilation and curettage | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus removal | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingo-oophorectomy bilateral | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Simple mastectomy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine artery embolisation | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal adhesiolysis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 2 / 347 (0.58%) | 2 / 349 (0.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion threatened | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical cord abnormality | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gestational hypertension | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Premature delivery | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Cervical cyst | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical polyp | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Pelvic adhesions | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal haematoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenomyosis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic discomfort | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysmenorrhoea | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 2 / 347 (0.58%) | 5 / 349 (1.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abnormal uterine bleeding | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic organ prolapse | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial hyperplasia with cellular atypia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Substance abuse | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biopsy peritoneum | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Norepinephrine increased | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scan adrenal gland abnormal | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia postoperative | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic fracture | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Venous angioma of brain | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRCA1 gene mutation | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal epidural haematoma | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 365 (0.55%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aplastic anaemia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 2 / 347 (0.58%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Primary hyperaldosteronism | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal mass | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid mass | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Synovitis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometritis | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mastitis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 1 / 347 (0.29%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 365 (0.27%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 1 / 349 (0.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 365 (0.00%) | 0 / 347 (0.00%) | 0 / 349 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Vilaprisan 2 mg A3 (3/2 regimen) - Post treatment AEs | Standard of care B - Post treatment AEs | |
|--|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 177 (15.25%) | 7 / 365 (1.92%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acoustic neuroma | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adrenal adenoma | | | |
| subjects affected / exposed | 2 / 177 (1.13%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 5 / 177 (2.82%) | 1 / 365 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian adenoma | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phyllodes tumour | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer female | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign mesenteric neoplasm | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive breast carcinoma | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine myoma expulsion | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign neoplasm of adrenal gland | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Degeneration of uterine leiomyoma | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Hysterectomy | | | |
| subjects affected / exposed | 8 / 177 (4.52%) | 1 / 365 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicectomy | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastectomy | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myomectomy | | | |
| subjects affected / exposed | 2 / 177 (1.13%) | 1 / 365 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingectomy | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hysterosalpingo-oophorectomy | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fusion surgery | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial ablation | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cyst removal | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medical device removal | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hysterosalpingectomy | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 1 / 365 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shoulder operation | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 1 / 365 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine dilation and curettage | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus removal | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingo-oophorectomy bilateral | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Simple mastectomy | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine artery embolisation | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal adhesiolysis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abortion threatened | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical cord abnormality | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abortion | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Premature delivery | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Cervical cyst | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical polyp | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Endometriosis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic adhesions | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal haematoma | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenomyosis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic discomfort | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic ovarian cyst | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abnormal uterine bleeding | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic organ prolapse | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial hyperplasia with cellular atypia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Substance abuse | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biopsy peritoneum | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Norepinephrine increased | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scan adrenal gland abnormal | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia postoperative | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic fracture | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Venous angioma of brain | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRCA1 gene mutation | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Dizziness | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal epidural haematoma | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central nervous system lesion | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aplastic anaemia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency anaemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 2 / 365 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Endocrine disorders | | | |
| Primary hyperaldosteronism | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adrenal mass | | | |
| subjects affected / exposed | 2 / 177 (1.13%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid mass | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Synovitis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometritis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 177 (0.00%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 177 (0.56%) | 0 / 365 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Vilaprisan 2 mg A1 (3/1 regimen) - Treatment emergent AEs | Vilaprisan 2 mg A2 (6/2 regimen) - Treatment emergent AEs | Vilaprisan 2 mg A3 (3/2 regimen) - Treatment emergent AEs |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 136 / 349 (38.97%) | 152 / 347 (43.80%) | 56 / 177 (31.64%) |
| Investigations | | | |
| Bone density decreased | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | 2 / 347 (0.58%) | 0 / 177 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 40 / 349 (11.46%) | 44 / 347 (12.68%) | 20 / 177 (11.30%) |
| occurrences (all) | 53 | 51 | 24 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 30 / 349 (8.60%) | 24 / 347 (6.92%) | 9 / 177 (5.08%) |
| occurrences (all) | 43 | 37 | 9 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 13 / 349 (3.72%) | 20 / 347 (5.76%) | 6 / 177 (3.39%) |
| occurrences (all) | 13 | 20 | 6 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 349 (1.15%) | 8 / 347 (2.31%) | 3 / 177 (1.69%) |
| occurrences (all) | 4 | 8 | 3 |
| Reproductive system and breast disorders | | | |
| Endometrial thickening | | | |
| subjects affected / exposed | 28 / 349 (8.02%) | 39 / 347 (11.24%) | 9 / 177 (5.08%) |
| occurrences (all) | 34 | 44 | 9 |
| Intermenstrual bleeding | | | |

| | | | |
|--|-------------------------|-------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 16 / 349 (4.58%) 26 | 24 / 347 (6.92%) 45 | 9 / 177 (5.08%) 15 |
| Heavy menstrual bleeding subjects affected / exposed occurrences (all) | 12 / 349 (3.44%) 13 | 10 / 347 (2.88%) 10 | 3 / 177 (1.69%) 3 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 37 / 349 (10.60%) 51 | 42 / 347 (12.10%) 55 | 14 / 177 (7.91%) 15 |

| Non-serious adverse events | Standard of care B - Treatment emergent AEs | Vilaprisan 2 mg A2 (6/2 regimen) - Post treatment AEs | Vilaprisan 2 mg A1 (3/1 regimen) - Post treatment AEs |
|--|---|---|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 90 / 365 (24.66%) | 67 / 347 (19.31%) | 75 / 349 (21.49%) |
| Investigations Bone density decreased subjects affected / exposed occurrences (all) | 1 / 365 (0.27%) 1 | 25 / 347 (7.20%) 25 | 27 / 349 (7.74%) 27 |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) | 0 / 365 (0.00%) 0 | 5 / 347 (1.44%) 5 | 3 / 349 (0.86%) 3 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 7 / 365 (1.92%) 13 | 2 / 347 (0.58%) 2 | 6 / 349 (1.72%) 6 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 18 / 365 (4.93%) 20 | 3 / 347 (0.86%) 3 | 2 / 349 (0.57%) 2 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 29 / 365 (7.95%) 30 | 12 / 347 (3.46%) 12 | 10 / 349 (2.87%) 10 |
| Reproductive system and breast disorders Endometrial thickening | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 13 / 365 (3.56%) 16 | 4 / 347 (1.15%) 4 | 2 / 349 (0.57%) 3 |
| Intermenstrual bleeding subjects affected / exposed occurrences (all) | 6 / 365 (1.64%) 8 | 10 / 347 (2.88%) 15 | 16 / 349 (4.58%) 34 |
| Heavy menstrual bleeding subjects affected / exposed occurrences (all) | 27 / 365 (7.40%) 30 | 6 / 347 (1.73%) 8 | 16 / 349 (4.58%) 21 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 12 / 365 (3.29%) 16 | 12 / 347 (3.46%) 16 | 14 / 349 (4.01%) 22 |

| Non-serious adverse events | Vilaprisan 2 mg A3 (3/2 regimen) - Post treatment AEs | Standard of care B - Post treatment AEs | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 44 / 177 (24.86%) | 14 / 365 (3.84%) | |
| Investigations Bone density decreased subjects affected / exposed occurrences (all) | 15 / 177 (8.47%) 15 | 6 / 365 (1.64%) 6 | |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) | 1 / 177 (0.56%) 1 | 0 / 365 (0.00%) 0 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 4 / 177 (2.26%) 4 | 0 / 365 (0.00%) 0 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 3 / 177 (1.69%) 3 | 2 / 365 (0.55%) 2 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 8 / 177 (4.52%) 8 | 1 / 365 (0.27%) 1 | |
| Reproductive system and breast | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| disorders | | | |
| Endometrial thickening | | | |
| subjects affected / exposed | 7 / 177 (3.95%) | 1 / 365 (0.27%) | |
| occurrences (all) | 7 | 1 | |
| Intermenstrual bleeding | | | |
| subjects affected / exposed | 2 / 177 (1.13%) | 3 / 365 (0.82%) | |
| occurrences (all) | 2 | 3 | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 8 / 177 (4.52%) | 1 / 365 (0.27%) | |
| occurrences (all) | 9 | 1 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 177 (2.26%) | 0 / 365 (0.00%) | |
| occurrences (all) | 4 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 13 June 2017 | - The protocol was amended to maintain consistency across vilaprisan Phase 3 studies and to reflect conclusions from data which was received from a drug-drug-interaction study. - The protocol was amended to exclude the use of strong CYP3A4 inducers. |
| 13 September 2017 | - Changes were implemented requested by health authorities (HA) and updated wording based on discussions with other Health Authorities and Ethic Committees deemed to provide further helpful clarification. - Prior and concomitant therapy was revised to minimize the risk that hormonal treatment was started before the endometrial biopsy was taken. - The visit description was revised to ensure that subjects who prematurely discontinue during the treatment phase got those gynecological examinations, including the cervical smear performed in order to make sure that they did not develop any abnormalities during the treatment. - Changes in hemoglobin were regarded as safety parameter and therefore the section on hemoglobin was added to the safety section. |
| 04 July 2018 | - Text added describing hepatic safety signal with Esmya (ulipristal acetate), a compound that belongs to the compound group of selective PRMs, and the result of the respective PRAC review procedure including risk minimization measures. (Recommendation by EMA Pharmacovigilance Risk Assessment Committee [PRAC] in May 2018.) - Description of increased frequency of liver monitoring and its background in subsection "safety monitoring" added. The criterion about abnormal liver parameters was revised. The diagnosis of chronic hepatitis B / C infection was added to exclusion criteria. A description for liver symptom inquiry was included. More detailed instructions for the monitoring of liver parameters and liver disorders and for close observation in cases with increased liver parameters and liver disorders were added. (To address FDA' requirement on more robust liver safety data and to closely align with specific feedback received in Jan and May 2018 and the 2009 FDA DILI guideline.) - A new exclusion criterion was added regarding a z-score of <-2 at baseline. More detailed instructions relating to the operative implementation of the new exclusion criterion regarding z-score were added, and clear instruction not to switch DEXA device during the study was included. (To address FDA feedback in May 2018.) - The sample size was increased from 1050 to 1302 (The increased sample size was to contribute to the database in which safety events of interest were to be evaluated.) |
| 20 August 2018 | - Update of mismatch between tables and visit descriptions to avoid site and Health Authority ambiguity. |
| 11 December 2018 | - Introduction of measures for the temporary pause of the study. |
| 21 November 2019 | - Introduction of measures and processes to prepare the study for an orderly closure. - Information on carcinogenicity studies with VPR in rodents as well as details regarding the additional safety measures were added, including adrenal monitoring, endometrial monitoring and skin monitoring. - Added text on additional analysis planned before the end of the study |
| 17 February 2020 | - The amendment addresses comments from the FDA regarding details of the safety follow-up measures introduced in protocol amendment 10, Version 7. - Described how subjects were counseled when test results (e.g., hormone, liver, physical examination) were abnormal but still below the thresholds to trigger outside evaluation in the context of the study. In such cases subjects were at least to be counseled about medical follow up according to local practice. - Revised the interval for blood sampling after intake of high doses of biotin from 8 to 72 hours. - Added glycosylated hemoglobin (HbA1c) to the parameters measured for adrenal monitoring also in subjects who had completed or discontinued the study before or during the temporary pause. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|---|--------------|
| 03 December 2018 | Bayer decided to temporarily pause enrollment and randomization, and to temporarily stop study treatment in already randomized patients after completion of the ongoing treatment period. | - |

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|--|
| The study ended prematurely. On top of the previous results after primary completion, adverse event data are added from long term follow-up of subjects in Turkey as per local requirements (5 years after individual end of study medication intake). |
|--|

Notes: