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	

Results information

Result version number	v1
This version publication date	14 September 2023
First version publication date	14 September 2023

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	Interim
Date of interim/final analysis	12 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 May 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study 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	Turkey: 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 10-May-2019 (Primary completion date).

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
Physician decision	6	9	5
Consent withdrawn by subject	69	72	34
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
Physician decision	4
Consent withdrawn by subject	131
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 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.

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			
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	8.7		
standard deviation	± 4.3	-	
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	1.1532		
standard deviation	± 0.1851	-	
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	0.9944		
standard deviation	± 0.1486	-	
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	0.9021		
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, B:11

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:

For TEAEs: From the first application of study medication up to 60 calendar days after end of treatment with study medication. For Post-treatment AEs: All AEs that started from Day 61 after the end of treatment with study medication.

Adverse event reporting additional description:

Treatment emergent adverse events = TEAEs

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

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 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 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 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
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
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
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
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
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
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

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
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
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
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
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			

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
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
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
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
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
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
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
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
Intestinal adhesion lysis			
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
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
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
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 leiomyoma 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
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
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
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
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
General disorders and administration site conditions			

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
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
Reproductive system and breast disorders			
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
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
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
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
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 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			
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 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
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
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
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
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
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
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
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
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
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
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

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
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
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
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
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
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
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
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
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
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
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
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
Traumatic 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
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
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
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
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
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			
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
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
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
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
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
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
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
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
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
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
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
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 A1 (3/1 regimen) - Post treatment AEs	Vilaprisan 2 mg A2 (6/2 regimen) - Post treatment AEs
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 365 (4.66%)	53 / 349 (15.19%)	41 / 347 (11.82%)
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 / 349 (0.00%)	0 / 347 (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%)	8 / 349 (2.29%)	2 / 347 (0.58%)
occurrences causally related to treatment / all	0 / 0	6 / 8	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	3 / 365 (0.82%)	3 / 349 (0.86%)	3 / 347 (0.86%)
occurrences causally related to treatment / all	0 / 3	1 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 365 (0.00%)	2 / 349 (0.57%)	0 / 347 (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
Breast cancer			
subjects affected / exposed	1 / 365 (0.27%)	1 / 349 (0.29%)	0 / 347 (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
Ovarian adenoma			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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 / 349 (0.00%)	0 / 347 (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	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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 myoma expulsion			

subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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 breast carcinoma			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 neoplasm of adrenal gland			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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			
Appendicectomy			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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
Hysterectomy			
subjects affected / exposed	2 / 365 (0.55%)	17 / 349 (4.87%)	15 / 347 (4.32%)
occurrences causally related to treatment / all	0 / 2	2 / 17	0 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastectomy			

subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	6 / 349 (1.72%)	4 / 347 (1.15%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingectomy			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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 ablation			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Hysterosalpingo-oophorectomy			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Hysterosalpingectomy			
subjects affected / exposed	0 / 365 (0.00%)	3 / 349 (0.86%)	0 / 347 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal adhesion lysis			

subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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
Shoulder operation			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 embolisation			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	1 / 347 (0.29%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingo-oophorectomy bilateral			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Simple mastectomy			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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 / 349 (0.57%)	2 / 347 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion threatened			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Umbilical cord abnormality			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Abortion			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Gestational hypertension			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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
Chest pain			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 polyp			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 cyst			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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 adhesions			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	1 / 349 (0.29%)	1 / 347 (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 prolapse			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Endometrial hyperplasia			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Uterine polyp			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Vaginal haematoma			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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
Adenomyosis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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%)	5 / 349 (1.43%)	2 / 347 (0.58%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 2
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%)	0 / 349 (0.00%)	1 / 347 (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
Pulmonary embolism			
subjects affected / exposed	1 / 365 (0.27%)	1 / 349 (0.29%)	0 / 347 (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
Dyspnoea exertional			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Pulmonary oedema			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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
Haemoglobin decreased			
subjects affected / exposed	1 / 365 (0.27%)	0 / 349 (0.00%)	0 / 347 (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
Biopsy peritoneum			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Scan adrenal gland abnormal			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Blood pressure increased			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Traumatic fracture			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Upper limb fracture			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Congenital, familial and genetic disorders			
Venous angioma of brain			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	1 / 347 (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
Nervous system disorders			
Cerebral infarction			

subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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			
Iron deficiency anaemia			

subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Aplastic anaemia			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Anaemia			
subjects affected / exposed	2 / 365 (0.55%)	0 / 349 (0.00%)	1 / 347 (0.29%)
occurrences causally related to treatment / all	0 / 2	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%)	1 / 349 (0.29%)	0 / 347 (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 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Large intestine polyp			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	2 / 347 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Gallbladder polyp			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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
Endocrine disorders			
Primary hyperaldosteronism			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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
Thyroid mass			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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%)	1 / 349 (0.29%)	0 / 347 (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
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 365 (0.27%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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%)	0 / 349 (0.00%)	1 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Pneumonia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 365 (0.00%)	1 / 349 (0.29%)	0 / 347 (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
Hyperglycaemia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 349 (0.00%)	0 / 347 (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 / 349 (0.00%)	0 / 347 (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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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			
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	
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	
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	
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	
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	
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	
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	
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	
Intestinal adhesion lysis			
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	
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	
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	
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 leiomyoma 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	
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	
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	
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	
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	
General disorders and administration site conditions			
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	
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	
Reproductive system and breast disorders			
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	

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	
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	
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	
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 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			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	

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	
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			
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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			
Intermenstrual bleeding			
subjects affected / exposed	16 / 349 (4.58%)	24 / 347 (6.92%)	9 / 177 (5.08%)
occurrences (all)	26	45	15
Endometrial thickening			

subjects affected / exposed	28 / 349 (8.02%)	39 / 347 (11.24%)	9 / 177 (5.08%)
occurrences (all)	34	44	9
Heavy menstrual bleeding			
subjects affected / exposed	12 / 349 (3.44%)	10 / 347 (2.88%)	3 / 177 (1.69%)
occurrences (all)	13	10	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	37 / 349 (10.60%)	42 / 347 (12.10%)	14 / 177 (7.91%)
occurrences (all)	51	55	15

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

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

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	15 / 177 (8.47%)	6 / 365 (1.64%)	
occurrences (all)	15	6	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 177 (0.56%)	0 / 365 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 177 (2.26%)	0 / 365 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 177 (1.69%)	2 / 365 (0.55%)	
occurrences (all)	3	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 177 (4.52%)	1 / 365 (0.27%)	
occurrences (all)	8	1	
Reproductive system and breast			

disorders			
Intermenstrual bleeding			
subjects affected / exposed	2 / 177 (1.13%)	3 / 365 (0.82%)	
occurrences (all)	2	3	
Endometrial thickening			
subjects affected / exposed	7 / 177 (3.95%)	1 / 365 (0.27%)	
occurrences (all)	7	1	
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.

Only two patients are in safety follow up due to local requirement.

Notes: