Clinical trial results:
A randomized, parallel-group, double-blind placebo-controlled and open label active-controlled, multi-center study to assess the efficacy and safety of vilaprisan in patients with uterine fibroids

Summary

EudraCT number	2014-004221-41
Trial protocol	SE DE PT NL GB FI AT CZ HU LT BE ES PL IT
Global end of trial date	26 October 2016

Results information

Result version number	v1 (current)
This version publication date	27 October 2017
First version publication date	27 October 2017

Trial information

Trial identification

Sponsor protocol code	BAY1002670/17541

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02465814
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy of vilaprisan in subjects with uterine fibroids compared to placebo.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all 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	01 June 2015
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	Netherlands: 4
Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Poland: 50
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Czech Republic: 29
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Lithuania: 10
Country: Number of subjects enrolled	Italy: 13

Worldwide total number of subjects	172
EEA total number of subjects	172

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)	172
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 47 study centers in Austria, Belgium, Bulgaria, Czech Republic, Finland, Germany, Hungary, Italy, Lithuania, Netherlands, Norway, Poland, Portugal, Spain, Sweden, and United Kingdom, between 01 June 2015 (first subject first visit) and 26 October 2016 (last subject last visit).

Pre-assignment

Screening details:

Overall, 244 subjects were screened, of them 72 subjects did not complete screening. A total of 172 subjects were randomized, of them 164 subjects received treatment in one of the 7 treatment arms and total 145 subjects completed the study.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The study included both double-blind, placebo-controlled and open label active-controlled parts. A double-blind placebo-controlled design was considered necessary to differentiate drug effects from the natural course of disease and background findings. An active comparator was considered appropriate to examine comparative efficacy and safety.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan

Arm description:

Subjects received 2 milligram (mg) oral dose of vilaprisan (BAY1002670) immediate release (IR) tablet once daily for 12 weeks during both the treatment periods 1 (TP1) and 2 (TP2). Treatment period 2 started on the day following the end of treatment period 1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during both TP1 and TP2.

Arm title	Treatment A2: Placebo + 2mg Vilaprisan

Arm description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started on the day following the end of TP1.

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

Dosage and administration details:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2.

Arm title	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan

Arm description:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during both TP1 and TP2.

Arm title	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan

Arm description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

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

Dosage and administration details:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2.

Arm title	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal

Arm description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Arm type	Experimental
Investigational medicinal product name	Ulipristal
Investigational medicinal product code	
Other name	Esmya 5 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during both TP1 and TP2.

Arm title	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal

Arm description:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1.

Investigational medicinal product name	Ulipristal
Investigational medicinal product code	
Other name	Esmya 5 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2.

Arm title	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo

Arm description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Arm type	Experimental
Investigational medicinal product name	Ulipristal
Investigational medicinal product code	
Other name	Esmya 5 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2.

Number of subjects in period 1	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan
Started	37	7	36
Completed treatment 1	33	6	35
Completed post – treatment 1	33	6	34
Completed treatment 2	32	6	31
Completed post – treatment 2	32	6	31
Completed	32	6	31
Not completed	5	1	5
Consent withdrawn by subject	1	1	3
Protocol violation	3	-	-
Protocol driven decision point	-	-	-
Other	-	-	1
Pregnancy	-	-	-
Adverse event	1	-	1

Number of subjects in period 1	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal
Started	8	39	7
Completed treatment 1	7	36	6
Completed post – treatment 1	7	31	6
Completed treatment 2	7	30	6
Completed post – treatment 2	7	30	6
Completed	7	30	6
Not completed	1	9	1
Consent withdrawn by subject	-	3	-
Protocol violation	-	1	1
Protocol driven decision point	-	2	-
Other	-	-	-
Pregnancy	-	1	-
Adverse event	1	2	-

Number of subjects in period 1	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo
Started	38
Completed treatment 1	32
Completed post – treatment 1	30
Completed treatment 2	27
Completed post – treatment 2	26

Completed	26
Not completed	12
Consent withdrawn by subject	4
Protocol violation	1
Protocol driven decision point	-
Other	1
Pregnancy	1
Adverse event	5

Period 2

Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan

Arm description:

Subjects received 2 milligram (mg) oral dose of vilaprisan (BAY1002670) immediate release (IR) tablet once daily for 12 weeks during both the treatment periods 1 (TP1) and 2 (TP2). Treatment period 2 started on the day following the end of treatment period 1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during both TP1 and TP2.

Arm title	Treatment A2: Placebo + 2mg Vilaprisan

Arm description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started on the day following the end of TP1.

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

Dosage and administration details:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2.

Arm title	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan

Arm description:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during both TP1 and TP2.

Arm title	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan

Arm description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

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

Dosage and administration details:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1.

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:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2.

Arm title	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal

Arm description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Arm type	Experimental
Investigational medicinal product name	Ulipristal
Investigational medicinal product code	
Other name	Esmya 5 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during both TP1 and TP2.

Arm title	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal

Arm description:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1.

Investigational medicinal product name	Ulipristal
Investigational medicinal product code	
Other name	Esmya 5 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2.

Arm title	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo

Arm description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Arm type	Experimental
Investigational medicinal product name	Ulipristal
Investigational medicinal product code	
Other name	Esmya 5 mg
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2.

Number of subjects in period 2	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan
Started	34	6	31
Completed	33	6	30
Not completed	1	0	1
Consent withdrawn by subject	1	-	-
Pregnancy	-	-	1

Number of subjects in period 2	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal
Started	7	34	6
Completed	7	34	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Pregnancy	-	-	-

Number of subjects in period 2	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo
Started	29
Completed	29
Not completed	0
Consent withdrawn by subject	-
Pregnancy	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan
Reporting group description:	
Subjects received 2 milligram (mg) oral dose of vilaprisan (BAY1002670) immediate release (IR) tablet once daily for 12 weeks during both the treatment periods 1 (TP1) and 2 (TP2). Treatment period 2 started on the day following the end of treatment period 1.	
Reporting group title	Treatment A2: Placebo + 2mg Vilaprisan
Reporting group description:	
Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started on the day following the end of TP1.	
Reporting group title	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan
Reporting group description:	
Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.	
Reporting group title	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan
Reporting group description:	
Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.	
Reporting group title	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal
Reporting group description:	
Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.	
Reporting group title	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal
Reporting group description:	
Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.	
Reporting group title	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo
Reporting group description:	
Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.	

Reporting group values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan
Number of subjects	37	7	36
Age categorical			
Units: subjects			

Age continuous			
Units: years			
arithmetic mean	40.9	42	43.5
standard deviation	± 6.5	± 2.8	± 4.4

Gender categorical Units: subjects			
Female	37	7	36
Menstrual blood loss volume for 28 days by menstrual pictogram			
Subjects documented their menstrual fluid loss per sanitary product (towels and/or tampons) using a visual scoring system for 28 days by menstrual pictogram.			
Units: milliliter (mL) arithmetic mean standard deviation	 246.938 ± 165.406	 238.393 ± 249.792	 206.523 ± 169.936
Menstrual blood loss volume for 35 days by menstrual pictogram			
Subjects documented their menstrual fluid loss per sanitary product (towels and/or tampons) using a visual scoring system for 35 days by menstrual pictogram.			
Units: milliliter (mL) arithmetic mean standard deviation	 247.003 ± 165.369	 238.393 ± 249.792	 207.605 ± 170.672
Volume of 3 largest fibroids by ultrasound			
The largest transverse, longitudinal, and antero-posterior diameters of these 3 fibroids were documented at each efficacy ultrasound examination for volume calculation.			
Units: milliliter (mL) arithmetic mean standard deviation	 104.549 ± 132.82	 100.302 ± 94.301	 100.278 ± 104.074
Uterine volume by ultrasound			
The dimensions of the uterus was calculated by using ultrasound examination.			
Units: milliliter (mL) arithmetic mean standard deviation	 228.798 ± 132.66	 315.548 ± 236.319	 320.839 ± 230.024

Reporting group values	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal
Number of subjects	8	39	7
Age categorical Units: subjects			
Age continuous Units: years arithmetic mean standard deviation	 43.1 ± 5.8	 41.5 ± 5.4	 40.3 ± 8.2
Gender categorical Units: subjects			
Female	8	39	7
Menstrual blood loss volume for 28 days by menstrual pictogram			
Subjects documented their menstrual fluid loss per sanitary product (towels and/or tampons) using a visual scoring system for 28 days by menstrual pictogram.			
Units: milliliter (mL) arithmetic mean standard deviation	 225.775 ± 90.95	 199.729 ± 101.5	 193.288 ± 81.259
Menstrual blood loss volume for 35 days by menstrual pictogram			
Subjects documented their menstrual fluid loss per sanitary product (towels and/or tampons) using a			

visual scoring system for 35 days by menstrual pictogram.			
Units: milliliter (mL)			
arithmetic mean	225.775	199.729	193.288
standard deviation	± 90.95	± 101.5	± 81.259
Volume of 3 largest fibroids by ultrasound			
The largest transverse, longitudinal, and antero-posterior diameters of these 3 fibroids were documented at each efficacy ultrasound examination for volume calculation.			
Units: milliliter (mL)			
arithmetic mean	94.811	119.713	134.645
standard deviation	± 113.219	± 135.195	± 114.341
Uterine volume by ultrasound			
The dimensions of the uterus was calculated by using ultrasound examination.			
Units: milliliter (mL)			
arithmetic mean	217.07	363.451	279.142
standard deviation	± 112.671	± 346.984	± 81.885

Reporting group values	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo	Total	
Number of subjects	38	172	
Age categorical			
Units: subjects			
Age continuous			
Units: years			
arithmetic mean	42.9		
standard deviation	± 5.2	-	
Gender categorical			
Units: subjects			
Female	38	172	
Menstrual blood loss volume for 28 days by menstrual pictogram			
Subjects documented their menstrual fluid loss per sanitary product (towels and/or tampons) using a visual scoring system for 28 days by menstrual pictogram.			
Units: milliliter (mL)			
arithmetic mean	200.89		
standard deviation	± 129.016	-	
Menstrual blood loss volume for 35 days by menstrual pictogram			
Subjects documented their menstrual fluid loss per sanitary product (towels and/or tampons) using a visual scoring system for 35 days by menstrual pictogram.			
Units: milliliter (mL)			
arithmetic mean	201.07		
standard deviation	± 128.951	-	
Volume of 3 largest fibroids by ultrasound			
The largest transverse, longitudinal, and antero-posterior diameters of these 3 fibroids were documented at each efficacy ultrasound examination for volume calculation.			
Units: milliliter (mL)			
arithmetic mean	98.742		
standard deviation	± 113.309	-	
Uterine volume by ultrasound			
The dimensions of the uterus was calculated by using ultrasound examination.			

Units: milliliter (mL)			
arithmetic mean	298.391		
standard deviation	± 216.267	-	

End points

End points reporting groups

Reporting group title	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan

Reporting group description:

Subjects received 2 milligram (mg) oral dose of vilaprisan (BAY1002670) immediate release (IR) tablet once daily for 12 weeks during both the treatment periods 1 (TP1) and 2 (TP2). Treatment period 2 started on the day following the end of treatment period 1.

Reporting group title	Treatment A2: Placebo + 2mg Vilaprisan

Reporting group description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started on the day following the end of TP1.

Reporting group title	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan

Reporting group description:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

Reporting group title	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan

Reporting group description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

Reporting group title	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal

Reporting group description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Reporting group title	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal

Reporting group description:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Reporting group title	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo

Reporting group description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Reporting group title	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan

Reporting group description:

Subjects received 2 milligram (mg) oral dose of vilaprisan (BAY1002670) immediate release (IR) tablet once daily for 12 weeks during both the treatment periods 1 (TP1) and 2 (TP2). Treatment period 2 started on the day following the end of treatment period 1.

Reporting group title	Treatment A2: Placebo + 2mg Vilaprisan

Reporting group description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started on the day following the end of TP1.

Reporting group title	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan

Reporting group description:

Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

Reporting group title	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan

Reporting group description:

Subjects received placebo matched to 2 mg vilaprisan IR tablet once daily for 12 weeks during TP1; followed by 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the first bleeding episode following the end of TP1.

Reporting group title	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal

Reporting group description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Reporting group title	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal

Reporting group description:

Subjects received placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP1; followed by 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Reporting group title	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo

Reporting group description:

Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during TP1; followed by placebo matched to 5 mg ulipristal IR tablet once daily for 12 weeks during TP2. Treatment period 2 started within the first 3 days of the second bleeding episode following the end of TP1.

Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

SAF (N=164) included all randomized subjects who took at least 1 dose of study drug. Subjects were analyzed as treated.

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

FAS (N=164) included all randomized subjects who took at least 1 dose of study drug. Subjects were analyzed as randomized.

Subject analysis set title	Vilaprisan 12 weeks-A1 (TP1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=35) received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks in treatment period 1.

Subject analysis set title	Vilaprisan 12 weeks-B1 (TP1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=35) received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks in treatment period 1.

Subject analysis set title	Ulipristal 12 weeks-C1 (TP1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=37) received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks in treatment period 1.

Subject analysis set title	Ulipristal 12 weeks-C3 (TP1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=37) received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks in treatment period 1.

Subject analysis set title	Placebo: Pooled A2, B2 and C2 (TP1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects (N=20) received placebo matched to vilaprisan and ulipristal IR tablets once daily for 12 weeks in treatment period 1.

Primary: Amenorrhea Rate

End point title	Amenorrhea Rate[1]

End point description:

Amenorrhea (yes or no) was defined as no scheduled or unscheduled bleeding/spotting after end of the initial bleeding episode until the end of the respective treatment period.

End point type	Primary

End point timeframe:

From start of the study treatment up to End of Treatment (12 weeks for groups B and C, 24 weeks for group A)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for the pooled placebo has been reported here instead of individual placebo groups.

End point values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Vilaprisan 12 weeks-A1 (TP1)	Vilaprisan 12 weeks-B1 (TP1)	Ulipristal 12 weeks-C1 (TP1)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35[2]	35[3]	35[4]	35[5]
Units: percentage of amenorrheic subjects				
number (confidence interval 95%)	25.71 (12.49 to 43.26)	57.14 (39.35 to 73.68)	62.86 (44.92 to 78.53)	59.46 (42.1 to 75.25)

Notes:

[2] - FAS

[3] - FAS

[4] - FAS

[5] - FAS

End point values	Ulipristal 12 weeks-C3 (TP1)	Placebo: Pooled A2, B2 and C2 (TP1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	35[6]	35[7]		
Units: percentage of amenorrheic subjects				
number (confidence interval 95%)	51.35 (34.4 to 68.08)	0 (0 to 16.84)		

Notes:

[6] - FAS

[7] - FAS

Statistical analyses

Statistical analysis title	Vilaprisan 12 weeks vs Placebo 12 weeks

Statistical analysis description:

Amenorrhea (yes or no) was defined as no scheduled or unscheduled bleeding/spotting after end of the initial bleeding episode until the end of the respective treatment period. The amenorrhea rates of vilaprisan vs placebo was analyzed using Fisher's exact tests at a 5% two sided significance level. A hierarchical (fixed sequence) testing procedure was used and 95% confidence intervals were calculated. P-value calculated with respect to Placebo 12 weeks.

Comparison groups	Vilaprisan 12 weeks-B1 (TP1) v Placebo: Pooled A2, B2 and C2 (TP1)

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher’s exact tests
Confidence interval	
level	95 %

Statistical analysis title	Vilaprisan 24 weeks vs Placebo 12 weeks

Statistical analysis description:

Amenorrhea (yes or no) was defined as no scheduled or unscheduled bleeding/spotting after end of the initial bleeding episode until the end of the respective treatment period. The amenorrhea rates of vilaprisan vs placebo was analyzed using Fisher’s exact tests at a 5% two sided significance level. A hierarchical (fixed sequence) testing procedure was used and 95% confidence intervals were calculated. P-value calculated with respect to Placebo 12 weeks.

Comparison groups	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan v Placebo: Pooled A2, B2 and C2 (TP1)
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Fisher’s exact tests
Confidence interval	
level	95 %

Secondary: Number of Bleeding Days

End point title	Number of Bleeding Days[8]

End point description:

Number of bleeding days from Day 1 of the first treatment period until the day before the next treatment period would start again normalized to 28 days. Arithmetic mean and standard deviation of bleeding days (normalized to 28 days) was reported.

End point type	Secondary

End point timeframe:

From Day 1 of the first treatment period until the day before the next treatment period (normalized to 28 days)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for the pooled placebo has been reported here instead of individual placebo groups.

End point values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Vilaprisan 12 weeks-A1 (TP1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	35[9]	35[10]	37[11]	35[12]
Units: bleeding days				
arithmetic mean (standard deviation)	1.69 (± 1.79)	1.46 (± 0.7)	2.05 (± 1.15)	1.54 (± 1.27)

Notes:

[9] - FAS

[10] - FAS

[11] - FAS

[12] - FAS

End point values	Vilaprisan 12 weeks-B1 (TP1)	Ulipristal 12 weeks-C1 (TP1)	Ulipristal 12 weeks-C3 (TP1)	Placebo: Pooled A2, B2 and C2 (TP1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35[13]	37[14]	37[15]	20[16]
Units: bleeding days				
arithmetic mean (standard deviation)	1.69 (± 0.8)	1.68 (± 1.13)	3.03 (± 4.7)	5.1 (± 1.62)

Notes:

[13] - FAS

[14] - FAS

[15] - FAS

[16] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Onset of Controlled Bleeding

End point title	Time to Onset of Controlled Bleeding

End point description:

Onset of controlled bleeding was defined based on the menstrual blood loss of all constructed moving evaluation time windows (METW) starting from the first day of treatment up to the end of treatment. Each completed METW was 28 days in length and each incomplete METW was less than 28 days. Onset of controlled bleeding was defined by the first day, for which the menstrual blood loss (MBL) assessed by menstrual pictogram for all subsequent 28-day periods up to the end of the treatment period was less than 80 mL. Kaplan-Meier estimated time to onset of controlled bleeding (days) was calculated and reported. In the below table, '99999' refers to data was not calculated as most subjects did not show controlled bleeding.

End point type	Secondary

End point timeframe:

From start of the study treatment up to 28 days

End point values	Vilaprisan 12 weeks-A1 (TP1)	Vilaprisan 12 weeks-B1 (TP1)	Ulipristal 12 weeks-C1 (TP1)	Ulipristal 12 weeks-C3 (TP1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35[17]	35[18]	37[19]	37[20]
Units: days				
median (inter-quartile range (Q1-Q3))	3 (2 to 4)	3 (2 to 4)	3 (1 to 4)	3 (2 to 4)

Notes:

[17] - FAS

[18] - FAS

[19] - FAS

[20] - FAS

End point values	Placebo: Pooled A2, B2			

	and C2 (TP1)			
Subject group type	Subject analysis set			
Number of subjects analysed	20[21]			
Units: days				
median (inter-quartile range (Q1-Q3))	99999 (33 to 99999)			

Notes:

[21] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Volume of Largest Fibroid

End point title	Percent Change From Baseline in Volume of Largest Fibroid

End point description:

Percent change in volume of largest fibroid compared to baseline measured by magnetic resonance imaging was reported.

End point type	Secondary

End point timeframe:

From start of the study treatment up to follow up period

End point values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29[22]	6[23]	28[24]	7[25]
Units: percent change				
arithmetic mean (standard deviation)				
TP1 (Treatment Visit 3) (n=29,6,28,7,31,6,29)	-27 (± 39.4)	-1.5 (± 22.3)	-29.6 (± 19.3)	9.1 (± 22.4)
TP2 (Treatment Visit 6) (n=27,6,27,7,29,6,25)	-35.6 (± 47.3)	-43.2 (± 14.7)	-47.6 (± 19)	-27 (± 18.8)
FUP period (FUP Visit) (n=23,6,23,7,26,5,25)	-39.2 (± 41.3)	-37.6 (± 28.1)	-36 (± 30.2)	-13 (± 29.9)

Notes:

[22] - FAS with evaluable subjects for this endpoint.

[23] - FAS

[24] - FAS with evaluable subjects for this endpoint.

[25] - FAS with evaluable subjects for this endpoint.

End point values	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[26]	6[27]	29[28]	
Units: percent change				

arithmetic mean (standard deviation)				
TP1 (Treatment Visit 3) (n=29,6,28,7,31,6,29)	-21.8 (± 30.2)	9 (± 12.2)	-25.2 (± 32.2)	
TP2 (Treatment Visit 6) (n=27,6,27,7,29,6,25)	-15.9 (± 46.4)	-2.6 (± 27.3)	-14.5 (± 28.9)	
FUP period (FUP Visit) (n=23,6,23,7,26,5,25)	-1.5 (± 59.9)	-1 (± 28.3)	-2 (± 35.6)	

Notes:

[26] - FAS with evaluable subjects for this endpoint.

[27] - FAS

[28] - FAS with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Endometrial Biopsy Results-at the End of Treatment Period 2

End point title	Number of Subjects With Endometrial Biopsy Results-at the End of Treatment Period 2

End point description:

Endometrial biopsies were assessed for immediate information about safety and for major consensus during the whole treatment phase. By endometrial biopsies pathologists documented proliferative / secretory / atrophic endometrium, endometrial hyperplasia.

End point type	Secondary

End point timeframe:

At the end of Treatment Period 2

End point values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[29]	5[30]	27[31]	7[32]
Units: subjects				
Benign Endometrium (Atrophic)	0	0	1	0
Benign Endometrium (Inactive)	1	0	0	1
Benign Endometrium (Proliferative)	12	3	19	2
Benign Endometrium (Secretory)	7	2	5	2
Benign Endometrium (Menstrual)	3	0	0	1
No Consensus	3	0	2	1
Endometrial Polyps (Functional)	0	0	2	0
No Endometrial Hyperplasia	26	5	27	7
No Malignant Neoplasm	26	5	27	7

Notes:

[29] - SAF with evaluable subjects for this endpoint.

[30] - SAF with evaluable subjects for this endpoint.

[31] - SAF with evaluable subjects for this endpoint.

[32] - SAF with evaluable subjects for this endpoint.

End point values	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25[33]	5[34]	22[35]	
Units: subjects				
Benign Endometrium (Atrophic)	2	0	0	
Benign Endometrium (Inactive)	1	0	0	
Benign Endometrium (Proliferative)	12	4	16	
Benign Endometrium (Secretory)	6	0	5	
Benign Endometrium (Menstrual)	0	0	0	
No Consensus	4	1	1	
Endometrial Polyps (Functional)	0	0	0	
No Endometrial Hyperplasia	25	5	22	
No Malignant Neoplasm	25	5	22	

Notes:

[33] - SAF with evaluable subjects for this endpoint.

[34] - SAF with evaluable subjects for this endpoint.

[35] - SAF with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Endometrial Biopsy Results-At the End of Follow-up Period

End point title	Number of Subjects With Endometrial Biopsy Results-At the End of Follow-up Period

End point description:

Endometrial biopsies were assessed for immediate information about safety and for major consensus during the whole treatment phase. By endometrial biopsies pathologists documented proliferative / secretory / atrophic endometrium, endometrial hyperplasia.

End point type	Secondary

End point timeframe:

At the end of Follow-up Period

End point values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[36]	5[37]	21[38]	5[39]
Units: subjects				
Benign Endometrium (Inactive)	2	0	0	0
Benign Endometrium (Proliferative)	13	2	17	4
Benign Endometrium (Secretory)	1	2	3	0
Benign Endometrium (Menstrual)	2	1	0	0
No Consensus	4	0	1	1

Endometrial Polyps (Functional)	0	0	0	0
No Endometrial Hyperplasia	22	5	21	5
No Malignant Neoplasm	22	5	21	5

Notes:

[36] - SAF with evaluable subjects for this endpoint.

[37] - SAF with evaluable subjects for this endpoint.

[38] - SAF with evaluable subjects for this endpoint.

[39] - SAF with evaluable subjects for this endpoint.

End point values	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20[40]	5[41]	23[42]	
Units: subjects				
Benign Endometrium (Inactive)	0	0	0	
Benign Endometrium (Proliferative)	16	4	16	
Benign Endometrium (Secretory)	1	0	3	
Benign Endometrium (Menstrual)	0	0	3	
No Consensus	3	1	1	
Endometrial Polyps (Functional)	1	0	0	
No Endometrial Hyperplasia	20	5	23	
No Malignant Neoplasm	20	5	23	

Notes:

[40] - SAF with evaluable subjects for this endpoint.

[41] - SAF with evaluable subjects for this endpoint.

[42] - SAF with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Endometrial Thickness Measured by Transvaginal Ultrasound

End point title	Endometrial Thickness Measured by Transvaginal Ultrasound

End point description:

Endometrial thickness weres measured by transvaginal ultrasound. Arithmetic mean and standard deviation were reported.

End point type	Secondary

End point timeframe:

Baseline, end of TP1, TP2 and Follow-up

End point values	Treatment A1: 2mg Vilaprisan + 2mg Vilaprisan	Treatment A2: Placebo + 2mg Vilaprisan	Treatment B1: 2mg Vilaprisan+1 Bleeding Episode+2mg Vilaprisan	Treatment B2: Placebo + 1 Bleeding Episode + 2mg Vilaprisan
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[43]	6[44]	35[45]	8[46]

Units: millimeter				
arithmetic mean (standard deviation)				
Baseline	8.97 (± 3.63)	7.5 (± 2.59)	7.51 (± 3)	6.75 (± 2.05)
At end of TP1	8.64 (± 4.47)	10.17 (± 3.37)	9.11 (± 4.78)	8.57 (± 4.47)
At end of TP2	10.24 (± 5.25)	10.5 (± 4.42)	7.88 (± 3.81)	7.86 (± 2.48)
At end of Follow-up	6.56 (± 2.78)	7 (± 2.53)	7.83 (± 3.11)	6.14 (± 2.55)

Notes:

[43] - SAF

[44] - SAF

[45] - SAF

[46] - SAF

End point values	Treatment C1:5mg Ulipristal+2 Bleeding Episodes+5mg Ulipristal	Treatment C2: Placebo + 2 Bleeding Episodes + 5mg Ulipristal	Treatment C3: 5mg Ulipristal + 2 Bleeding Episodes + Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37[47]	6[48]	37[49]	
Units: millimeter				
arithmetic mean (standard deviation)				
Baseline	7.7 (± 2.46)	8.33 (± 3.01)	8.22 (± 2.96)	
At end of TP1	9.38 (± 5.16)	8.17 (± 3.6)	9 (± 4.74)	
At end of TP2	7.29 (± 3.35)	7.67 (± 4.32)	8.7 (± 3.07)	
At end of Follow-up	7.42 (± 3.92)	8.5 (± 5.58)	8.14 (± 2.46)	

Notes:

[47] - SAF

[48] - SAF

[49] - SAF

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study drug administration up to 12 weeks after the end of the treatment period 2 (Week 36)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	2 mg Vilaprisan
Reporting group description:	
2 mg Vilaprisan: Subjects received 2 mg oral dose of vilaprisan IR tablet once daily for 12 weeks during both the TP1 and TP2, or only during TP2.	
Reporting group title	5 mg Ulipristal
Reporting group description:	
5 mg Ulipristal: Subjects received 5 mg oral dose of ulipristal IR tablet once daily for 12 weeks during both the TP1 and TP2, or only during TP1, or only during TP2.	
Reporting group title	Placebo
Reporting group description:	
Placebo: Subjects received placebo matched to 2 mg vilaprisan or 5 mg ulipristal IR tablet once daily for 12 weeks.	

Serious adverse events	2 mg Vilaprisan	5 mg Ulipristal	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 83 (3.61%)	4 / 80 (5.00%)	0 / 50 (0.00%)
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)			
Haemangioma of bone			
subjects affected / exposed	0 / 83 (0.00%)	1 / 80 (1.25%)	0 / 50 (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 / 83 (0.00%)	1 / 80 (1.25%)	0 / 50 (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
General disorders and administration site conditions			

Surgical failure			
subjects affected / exposed	0 / 83 (0.00%)	1 / 80 (1.25%)	0 / 50 (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			
Menorrhagia			
subjects affected / exposed	1 / 83 (1.20%)	0 / 80 (0.00%)	0 / 50 (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 pain			
subjects affected / exposed	0 / 83 (0.00%)	1 / 80 (1.25%)	0 / 50 (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 haemorrhage			
subjects affected / exposed	1 / 83 (1.20%)	0 / 80 (0.00%)	0 / 50 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 83 (1.20%)	0 / 80 (0.00%)	0 / 50 (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

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

Non-serious adverse events	2 mg Vilaprisan	5 mg Ulipristal	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 83 (53.01%)	44 / 80 (55.00%)	17 / 50 (34.00%)
Investigations			
Weight increased			
subjects affected / exposed	6 / 83 (7.23%)	1 / 80 (1.25%)	0 / 50 (0.00%)
occurrences (all)	6	1	0
Vascular disorders			
Hot flush			

subjects affected / exposed	10 / 83 (12.05%)	5 / 80 (6.25%)	1 / 50 (2.00%)
occurrences (all)	13	5	2
Nervous system disorders			
Headache			
subjects affected / exposed	21 / 83 (25.30%)	18 / 80 (22.50%)	9 / 50 (18.00%)
occurrences (all)	34	19	11
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 83 (1.20%)	1 / 80 (1.25%)	3 / 50 (6.00%)
occurrences (all)	1	1	3
Ovarian cyst			
subjects affected / exposed	1 / 83 (1.20%)	12 / 80 (15.00%)	1 / 50 (2.00%)
occurrences (all)	2	15	2
Pelvic pain			
subjects affected / exposed	4 / 83 (4.82%)	4 / 80 (5.00%)	1 / 50 (2.00%)
occurrences (all)	4	4	1
Vaginal haemorrhage			
subjects affected / exposed	6 / 83 (7.23%)	3 / 80 (3.75%)	0 / 50 (0.00%)
occurrences (all)	6	3	0
Endometrial thickening			
subjects affected / exposed	5 / 83 (6.02%)	7 / 80 (8.75%)	0 / 50 (0.00%)
occurrences (all)	5	7	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	5 / 83 (6.02%)	0 / 80 (0.00%)	0 / 50 (0.00%)
occurrences (all)	5	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 83 (6.02%)	3 / 80 (3.75%)	1 / 50 (2.00%)
occurrences (all)	5	3	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 83 (7.23%)	11 / 80 (13.75%)	5 / 50 (10.00%)
occurrences (all)	6	11	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2015	After the European Union label of the active reference drug Esmya (ulipristal acetate 5 mg tablets) had been changed, the former labelled indication of short-term use of Esmya before surgical treatment of uterine fibroids was extended to repeated intermittent use. Consequently, the inclusion criterion "Eligible to undergo surgical treatment for uterine fibroids at the end of study treatment" and related protocol sections could be deleted.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Occurrence of "±" in relation with geometric CV is auto-generated and cannot be deleted. Decimal places were automatically truncated if last decimal equals zero.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28185997