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

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Menstrual cycle and uterine bleeding disorders
Study type	Interventional

Summary

ID

NL-OMON42795

Source
ToetsingOnline

Brief title
Assess safety and efficacy of vilaprisan in patients with uterine fibroids

Condition

- Menstrual cycle and uterine bleeding disorders

Synonym
leiomyoma, uterine fibroids

Research involving

Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer healthcare AG

Intervention

Keyword: heavy menstrual bleeding, uterine fibroids

Outcome measures

Primary outcome

To assess the efficacy of vilaprisan in subjects with uterine fibroids

compared to placebo

Secondary outcome

To assess the efficacy of vilaprisan in subjects with uterine fibroids compared

to ulipristal.

Study description

Background summary

Uterine fibroids are the leading cause for hysterectomy. Hysterectomy is the only definitive treatment and eliminates the possibility of recurrence. In North America, 275,000 women per year undergo hysterectomy as uterine fibroid treatment. Many women seek an alternative to hysterectomy because they desire future childbearing or wish to retain their uterus. For women who desire uterine preservation, myomectomy is an alternative surgical procedure. The goal is to remove visible and accessible fibroids and reconstruct the uterus. However, the recurrence rate is substantial and up to 25% of patients require repeat myomectomy or hysterectomy at a later stage. The medical need for pharmacological alternatives to surgical or interventional treatment options is considered high.
The selective progesterone receptor modulator vilaprisan (BAY 1002670) is a promising new drugcandidate for the long-term treatment of uterine fibroids. Evidence for efficacy is based on the clinical experience with other progesterone receptor modulators, the potencies and selectivities of which are

lower compared to vilaprisan. If its pharmacologic properties can be translated into significant therapeutic efficacy, options for medical treatment of symptomatic uterine fibroids would considerably improve.

Study objective

The primary objective of this study is
• To assess the efficacy of vilaprisan in subjects with uterine fibroids compared to placebo.
The secondary objectives of this study are
• To assess the efficacy of vilaprisan in subjects with uterine fibroids compared to ulipristal.
• To evaluate the safety of vilaprisan in subjects with uterine fibroids.

Study design

Randomized, parallel-group, double-blind, placebo-controlled and open label active-controlled, multi-center design Screening period of up to 60 days.
Eligible subjects will be randomized to one of the following treatment groups:
Treatment groups A1, B1, C1, C3: 30 subjects each
Treatment groups A2, B2, C2: 6 subjects each

• A1: Vilaprisan 2 mg (12 weeks), vilaprisan 2 mg (12 weeks)
• A2: Placebo (12 weeks), vilaprisan 2 mg (12 weeks).

• B1: Vilaprisan 2 mg (12 weeks), 1 bleeding episode, vilaprisan 2 mg (12 weeks).
• B2: Placebo (12 weeks), 1 bleeding episode, vilaprisan 2 mg (12 weeks).

• C1: Ulipristal 5 mg (12 weeks), 2 bleeding episodes , ulipristal 5 mg (12 weeks)
• C2: Placebo (12 weeks), 2 bleeding episodes, ulipristal 5 mg (12 weeks)
• C3: Ulipristal 5 mg (12 weeks), 2 bleeding episodes, placebo (12 weeks)

After the end of treatment, subjects will be followed up for 12 weeks.

Intervention

A1: Vilaprisan 2 mg (12 weeks), vilaprisan 2 mg (12 weeks)
A2: Placebo (12 weeks), vilaprisan 2 mg (12 weeks).

B1: Vilaprisan 2 mg (12 weeks), 1 bleeding episode, vilaprisan 2 mg (12 weeks).
B2: Placebo (12 weeks), 1 bleeding episode, vilaprisan 2 mg (12 weeks).

C1: Ulipristal 5 mg (12 weeks), 2 bleeding episodes , ulipristal 5 mg (12

weeks)
C2: Placebo (12 weeks), 2 bleeding episodes, ulipristal 5 mg (12 weeks)
C3: Ulipristal 5 mg (12 weeks), 2 bleeding episodes, placebo (12 weeks)

Study burden and risks

Patients have to undergo 10 site visits,
- 3 during the screening phase which is aimed to verify the inclusion and exclusion criteria
- 6 visits during treatment (3 visits per treatment period)
- and a final visit at the end of the follow up period of 12 weeks.
The study duration for a single patient will be 12-13 months depending on the treatment group.The following procedures are planned:
- 7 times blood samples for safety assessments and 4 times for PK - total blood amount about 150 ml - During the collection of blood samples, pain and/or bruising may occur at the needle site. Occasionally, an infection may occur around the blood drawing site. An infection
may sometimes involve the vein and may on rare occasions be very serious and require surgery. Lightheadedness and/or fainting occasionally occur during, or shortly after, blood is drawn.
- 4 physical and 3 gynecological examinations
- transvaginal ultrasound at all visits
- cervical smear sampling at baseline and follow up - may cause discomfort and spotting
- endometrial biopsy sampling at 3 visits - While the procedure is generally considered safe, cramps or pelvic pain are common short-lived side effects. If required painkillers can be used (please discuss with your study doctor). After the procedure, you may experience some bleeding. A uterine perforation or infection is a rare complication. Since a biopsy should not be taken during pregnancy, a urine pregnancy test will be taken before each biopsy
- 4 times magnetic resonance imaging (MRI) without contrast agent

Throughout the whole study duration, patients are requested to use non-hormonal methods of barrier contraception, Pregnancy tests will be performed at each visit. A daily electronic diary has to be filled in.
The following side effects have been reported with the study drug in previous studies:
For >10% of subjects of the overall study population after single or multiple dosing with study drug, mild or moderate headache was reported. Less frequently reported side effects >3% and <10% of subjects included nausea, fatigue and hot flush. Ovarian cysts were observed during and after treatment in 11% of women of reproductive age, and most of the cases spontaneously disappeared within a few weeks. Less frequently were abdominal pain, menstrual cramps, and uterine disorders. Transient ECG alterations at different dose levels without clinical relevance were registered in some subjects. In less than 10% of the subjects taking doses of the study drug, as compared to this study, liver parameters were slightly above the reference range. Therefore, a close control

of liver parameters will take place during this study.
Due to the low number of study subjects who have taken the study drug so far, the following side effects might be expected due to the nature of the study drug and based on results from studies with drugs in the same compound class:
Endometrial changes: The inner lining of the uterus (endometrium) may thicken or other changes in the endometrium may appear as a result of taking the study drug. These changes are expected to disappear after treatment is stopped and menstrual periods restart.
There can be no certainty that a patient will have any benefit from the study drug, however it is expected that the study drug may decrease heavy menstrual blood loss, other fibroid related symptoms, and fibroid size. The information the study sponsor receives from this study may help to develop a better long term treatment for uterine fibroid patients and to define the optimal dose of the drug.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Signed and dated informed consent;2. Women, 18 to 50 years of age at the time of screening;3. Diagnosis of uterine fibroid(s) documented by transvaginal or abdominal ultrasound at screening with at least 1 fibroid with largest diameter >/=3.0 cm;4. Heavy menstrual bleeding (HMB) > 80 mL documented by menstrual pictogram (MP) in a bleeding episode during the screening period;Women who did not suffer from perceived HMB during the 3 months prior to Visit 1 due to any effective medical treatment, e.g. with a hormonal contraceptive, are not considered appropriate candidates and should not undergo further screening procedures.;Women suffering from perceived HMB despite medical treatment, e.g. with a hormonal contraceptive, are appropriate candidates for further screening, if rules on stopping prior medication are followed.;5. Good general health (except for findings related to uterine fibroids) as proven by medical history, physical and gynecological examinations, and laboratory test results;6. Normal or clinically insignificant cervical smear not requiring further follow-up. Human papilloma virus (HPV) testing in subjects with atypical squamous cells of undetermined significance (ASCUS) can be used as an adjunctive test. Subjects with ASCUS can be included if they are negative for high-risk HPV strains.;7. An endometrial biopsy performed during the screening period, without significant histological disorder such as endometrial hyperplasia (including simple hyperplasia) or other significant endometrial pathology.;8. Use of an acceptable nonhormonal method of contraception (i.e. either male condom, cap, diaphragm or sponge, each in combination with spermicide) starting at the bleeding episode following the screening visit 1 (Visit 1) until the end of the study. This is not required if safe contraception is achieved by a permanent method, such as bilateral fallopian tube blockage of the subject or vasectomy of the partner(s).

Exclusion criteria

1. Pregnancy or lactation (less than 3 months since delivery, abortion, or lactation before start of treatment);2. Uterine fibroid with largest diameter > 10.0 cm;3. Hypersensitivity to any ingredient of the study drugs;4. Hemoglobin values

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-08-2015
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BAY1002670
Generic name:	vilaprisan
Product type:	Medicine
Brand name:	Esmya
Generic name:	ulipristal
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-04-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-06-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-07-2015

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-08-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-004221-41-NL
CCMO	NL52878.100.15