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Mifepristone 50 mg as a weekly contraceptive

Submission date
15/02/2021

Recruitment status
Recruiting

Registration date
24/02/2021

Overall study status
Ongoing

Last Edited
25/10/2024

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Satisfying the unmet need for contraception could prevent 79,000 maternal deaths and 1.1 million infant deaths each year and lead to better health, social and economic for mothers and children. Research on women's reasons for not using contraceptives suggests a need for new methods that are more in line with women's needs and preferences. The most common reason that women do not use modern contraceptives is because of concerns about health risks and side effects.

The contraceptive properties of mifepristone are well documented but further studies are required to develop and market this medicine as a contraceptive. In trials conducted in China, a weekly dose of 25 mg mifepristone was compared to 50 mg. No pregnancies occurred in 234 menstrual cycles of women who took weekly mifepristone 25 mg, and in 222 menstrual cycles of women who used mifepristone 50 mg as their only contraceptive.

This study aims to determine the safety of long-term use of once-a-week mifepristone 50 mg and its efficacy in preventing pregnancy. Safety assessments will focus on liver function and non-cancerous changes to the endometrium. Additionally, the study will assess the side-effects of weekly mifepristone 50 mg.

Who can participate?
Women aged 18 to 35 years old who are not planning to become pregnant within the next 13 months and are willing to use the study drug as only method of contraception over the course of the study period.

What does the study involve?
Participation in the study will last approximately 15 months (15 menstrual cycles) or until its termination due to safety concerns or other reasons. Women who participate in the study will take one tablet of mifepristone 50 mg each week for a treatment period of 13 months. Participants will visit study doctors a total of 6 times over the course of the study for monitoring (once every 3 months), including a visit 2 months after the treatment period is complete.

The effectveness of the treatment as a contraceptive will be assessed by measuring the number of pregnancies that occur during the treatment period. Pregnancy will be determined both by participants themselves, every 4 weeks and by study doctors every 3 months using tests of urine

samples. THe safety of the treatment will be assessed by blood tests to monitor liver function, and vaginal ultrasounds and endometrial biopsies (in a subset of volunteers) to assess endometrial changes. Information concerning side effects will be recorded by participants using daily diary cards and questionnaires relating to their quality of life and sexual function.

What are the possible benefits and risks of participating?
The study will be conducted in Georgia where mifepristone 50 mg is already available in pharmacies for the treatment of myoma.

All drugs may cause side effects in some individuals. Every participant will be closely monitored with respect to any side effects. Unknown reactions can also develop. For example, some drugs may induce allergic reactions in certain patient groups. During treatment with mifepristone, the following side-effects may occur irregular menstrual cycle, amenorrhea (no menstrual bleeding), oligomenorrhea (not much bleeding), light or moderate gastrointestinal cramping, light or moderate headache, feeling sick (nausea), vomiting, diarrhoea, dizziness, fever, feeling of weakness or allergic reactions (skin rash, urticaria). The long-term use of mifepristone can cause changes in the lining of the womb. These changes are not malignant. Very rarely, medicines similar to mifepristone may be associated with negative effects on liver function.

As with all forms of contraceptives, there is a small chance that a person may become pregnant during the study. If the participant becomes pregnant and chooses to carry the pregnancy to term, there is a risk of miscarriage. Additionally, there is a very small increased risk of foetal malformations after using mifepristone.

Where is the study run from?
Women on Waves. Clinics across Moldova will participate in the study.

When is the study starting and how long is it expected to run for?
January 2019 to June 2028

Who is funding the study?
Several funders

Who is the main contact?
Women on Waves
gomperts@womenonwaves.org

Contact information

Type(s)
Public

Contact name
Dr Rebecca Gomperts

Contact details
Women on Waves
Domselaerstraat 14
Amsterdam
Netherlands
1093MA

-
gomperts@womenonwaves.org

Type(s)
Scientific

Contact name
Prof Kristina Gemzell Danilelsson

Contact details
Widerströmska huset
Tomtebodavägen 18A 8th floor
Stockholm
Sweden
SE-171 77
+46 851772128
kristina.Gemzell@ki.se

Additional identifiers

EudraCT/CTIS number
2020-002355-38

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
mife50

Study information

Scientific Title
Prospective multi-center single arm open label study of efficacy, safety and acceptability of longterm weekly oral Mifepristone 50 mg as contraceptive

Acronym
Mife50

Study objectives
Once a week mifepristone 50 mg as a contraceptive has a Pearl Index of less than 1 and that a weekly 50 mg dose does not pose a safety risks after 13 cycles of use.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Current ethics details as of 10/10/2023:
Approved 24/05/2022, MMDA (str korolenko 1/2, chisinau, MD-2028, Moldova; +35322884301; office@amed.md), ref: RG03-000049

Previous ethics details:
Approved 27/12/2019, amendment approved 15/12/2020, Health Research Union (47 Tashkenti Street, Tbilisi 0177, Georgia; info@hru.ge; +995 32 2144447; info@hru.ge), ref: 2019-10, amendment ref: 2020-13

Study design
This interventional study is an open-label single-arm combined Phase II/III trial. All participants will be administered once a week mifepristone 50 mg (Ginestril®) for 13 menstrual cycles (approximately 13 months).

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Prevention of unwanted pregnancy

Interventions
Current interventions as of 10/10/2023:

All participants will self-administer one Ginestril 50 mg tablet (mifepristone 50 mg) per week orally for a duration of 15 menstrual cycles, or until its termination due to safety concerns or other reasons.

Participants will visit study doctors a total of 6 times over the course of the study for monitoring (once every 3 months), . The effectiveness of the treatment as a contraceptive will be assessed by measuring the number of pregnancies that occur during the treatment period. Pregnancy will be determined both by participants themselves every 4 weeks. The safety of the treatment will be assessed by blood tests to monitor liver function. Endometrial changes will be assessed using vaginal ultrasounds and endometrial biopsies at the beginning and end of the study. Informationconcerning side effects will be recorded by participants using daily diary cards and questionnaires relating to their quality of life and sexual function.

Previous interventions as of 16/06/2022:

All participants will self-administer one Ginestril 50 mg tablet (mifepristone 50 mg) per week orally for a duration of 15 menstrual cycles, or until its termination due to safety concerns or other reasons.

Participants will visit study doctors a total of 6 times over the course of the study for monitoring (once every 3 months), including a visit 2 months after the treatment period is complete. The effectiveness of the treatment as a contraceptive will be assessed by measuring the number of pregnancies that occur during the treatment period. Pregnancy will be determined both by participants themselves every 4 weeks and by study doctors every 3 months using tests of urine human chorionic gonadotropin (hCG). The safety of the treatment will be assessed by blood tests to monitor liver function. Endometrial changes will be assessed using vaginal ultrasounds and endometrial biopsies at the beginning and end of the study. Information concerning side effects will be recorded by participants using daily diary cards and questionnaires relating to their quality of life and sexual function.

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All participants will self-administer one Ginestril 50 mg tablet (mifepristone 50 mg) per week orally for a duration of 15 menstrual cycles, or until its termination due to safety concerns or other reasons.

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Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
mifepristone 50 mg tablets

Primary outcome measure
Current primary outcome measure as of 10/10/2023:

1. Occurrence of pregnancy during treatment
2. Endometrial changes
3. SEA's

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Previous primary outcome measure:

1. Occurrence of pregnancy during treatment caused by method failure measured using the following:
1.1. Participant administered urine hCG pregnancy tests every 4 weeks between baseline and 15 months
1.2. Investigator administered urine hCG pregnancy tests at baseline, 3, 6, 9, 13, and 15 months
1.3. Vaginal ultrasound at baseline, 3, 6, 9, 13, and 15 months
1.4. Self-reporting of adherence in participant diaries between baseline and 13 months
2. Proportion of women with endometrium thickness >15 mm and/or an endometrium with an irregular cystic appearance measured using vaginal ultrasound at baseline, 3, 6, 9, 13, and 15 months
3. Proportion of women with ALAT, ASAT, and bilirubin elevation three times above normal measured using blood tests at baseline, 3, 6, 9, 13, and 15 months
4. Proportion of women with adverse events and serious adverse events from case report forms completed by investigators between baseline and 15 months

Secondary outcome measures

Current secondary outcome measures as of 10/10/2023:

Acceptablility

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Previous secondary outcome measures:

1. Occurrence of pregnancy during treatment caused by user failure measured using the following:
1.1. Participant administered urine hCG pregnancy tests every 4 weeks between baseline and 15 months
1.2. Investigator administered urine hCG pregnancy tests at baseline, 3, 6, 9, 13, and 15 months
1.3. Vaginal ultrasound at baseline, 3, 6, 9, 13, and 15 months
1.4. Self-reporting of adherence in participant diaries between baseline and 13 months
2. Proportion of women with blood hormone levels abnormalities measured using blood test at baseline, 3, 6, 9, 13, and 15 months
3. Proportion of women with endometrial changes (PAEC) confirmed by endometrial biopsy at baseline, 3, 6, 9, 13, and 15 months
4. Proportion of women with normal haemoglobin value measured using blood tests at baseline, 3, 6, 9, 13, and 15 months
5. Quality of life measured using the mean value of the EuroQol 5-dimension quality of life questionnaire (EQ-5D-5L) at baseline, 3, 6, 9, 13, and 15 months
6. Proportion of women who uses antidepressants measured from participant diaries between baseline and 15 months
7. Proportion of women with dysmenorrhea measured from participant diaries between baseline and 15 months
8. Proportion of women with acne occurrence measured from participant diaries between baseline and 15 months
9. Proportion of women with side-effects (such as headache, nausea, breast pain, dry eyes) measured from participant diaries between baseline and 15 months
10. Weight measured using a scale at baseline, 3, 6, 9, 13, and 15 months

11. Proportion of women with vaginal bleeding measured from participant diaries between baseline and 15 months
12. Libido measured using the mean value of Female Sexual Function Index (FSFI) at baseline, 3, 6, 9, 13, and 15 months

Overall study start date
01/01/2019

Completion date
01/06/2028

Eligibility

Key inclusion criteria
1. No desire to become pregnant within the next 13 months
2. Provision of signed and dated informed consent form for participation in the study
3. Willing to comply with all study procedures and available for the duration of the study
4. Aged between 18 and 35 years
5. Have a normal menstrual cycle length between 25 and 35 days
6. At least one normal menstrual cycle after miscarriage or abortion and no abnormal blood loss
7. Willing to engage in at least three acts of penis-in-vagina sexual intercourse per month
8. Willing to use the study drug as the only method of contraception over the course of the study. If the potential participant is taking another contraceptive, they would have to stop and have one menstruation to be included in the trial.
9. Able to take oral medication and be willing to adhere to the contraceptive regimen

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Female

Target number of participants
949

Key exclusion criteria
1. Current pregnancy
2. Within 3 months of delivery
3. Abnormal cervical smear or within the year before
4. Known infertility or subfertility
5. History of ectopic pregnancy

6. Any previous or current malignancy including breast cancer
7. Abnormal liver enzymes
8. Irregularities in the endometrium
9. Retained products of conception after miscarriage or abortion
10. Signs of endometritis
11. Known allergic reactions to mifepristone
12. Lactation
13. Using high doses of corticosteroids or any drugs that may interact with mifepristone including hydantoins (e.g. phenytoin), barbiturates (e.g. phenobarbital), primidone, carbamazepine, rifampicin, oxcarbazepine, topiramate, rifabutin, felbamate, ritonavir, nelfinavir, griseofulvin, and products containing St. John's wort (Hypericum perforatum)
14. Treatment with another investigational drug
15. Unable to comply with the trial protocol

Date of first enrolment
01/10/2023

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
Moldova

Study participating centre
Reproductive Health Training Center (RHTC)
Chisinau
Moldova
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Sponsor information

Organisation
Women on Waves

Sponsor details
Domselaerstraat 14
Amsterdam
Netherlands
1093 MA
+31204650004
info@womenonwaves.org

Sponsor type

Charity

Website
https://www.womenonwaves.org/en/

Funder(s)

Funder type
Other

Funder Name
Funded by anonymous individual donors

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/01/2028

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date