

# Efficacy of mifepristone followed by misoprostol compared to misoprostol alone in first-trimester miscarriage treatment

<b>Submission date</b> 04/09/2020	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 12/09/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 31/07/2023	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

First-trimester miscarriage (FTM) is the loss of a pregnancy during the first 13 weeks of pregnancy. It is a common event, occurring in 10 to 15% of all clinically identified pregnancies. Medical treatment of FTM allows a more predictable expulsion of products of conception compared to expectant management (waiting for the miscarriage to happen by itself naturally) and avoid the risks of surgical management. Misoprostol is a drug that is widely used for that effect. Vaginal administration of 800 µg is the most suitable treatment as a single dose, with success rates reaching 85%. Several studies have been investigating the combination of mifepristone with misoprostol in FTM and suggest an improvement in success rates compared to misoprostol alone. The aim of this study is to assess the effectiveness of mifepristone plus misoprostol compared to misoprostol alone for FTM.

### Who can participate?

Healthy women aged 18 years or older diagnosed with FTM up to 9 weeks of gestation

### What does the study involve?

Participants start the treatment under a physician's supervision, taking orally a single-dose numbered white pill, which can contain 200 mg of either mifepristone or placebo. Participants will be randomly allocated to take mifepristone or placebo. Participants are instructed to complete the treatment with 800 µg of vaginal misoprostol 36 to 48 hours after the oral pill and another visit is scheduled in 2 to 3 weeks at the same service but not necessarily with the same physician. Demographic and clinical information is collected. The participants receive written information about FTM and medical treatment. They also complete a questionnaire about their experience, including date and time of misoprostol administration, adverse effects (nausea, vomiting, diarrhea, headache, dizziness, chills or fever), bleeding and pain intensity, pain medication use and acceptability. Vaginal misoprostol can be repeated about 48 hours later if no tissue is lost or if missed or incomplete miscarriage is diagnosed in follow-up. In each follow-up the physician performs a gynaecological exam and transvaginal ultrasound, reports symptoms or complications and the conduct adopted. In the center where the trial takes place it is common practice to reserve aspiration/curettage as a last-line treatment, although that possibility is

always discussed with the patients. All participants are followed up until miscarriage resolution (diagnosis of complete miscarriage or surgical treatment).

What are the possible benefits and risks of participating?

Many Portuguese public hospitals offer only misoprostol for FTM treatment. Half of the study participants receive mifepristone, which may have a higher success rate. The surveillance and health care offered to participants is similar to any patient diagnosed with FTM. The combination with mifepristone (200 mg) is considered safe and none of the previously referred studies reported an increased risk of adverse events compared to misoprostol alone.

Where is the study run from?

Hospital Senhora da Oliveira – Guimarães (Portugal)

When is the study starting and how long is it expected to run for?

December 2018 to December 2021

Who is funding the study?

Hospital Senhora da Oliveira – Guimarães (Portugal)

Who is the main contact?

Beatriz Bettencourt Silva

beatrizbettsilva@gmail.com

## Contact information

### Type(s)

Scientific

### Contact name

Dr Beatriz Bettencourt Silva

### ORCID ID

<https://orcid.org/0000-0002-1743-4329>

### Contact details

Rua dos Cutileiros, Creixomil

Hospital Senhora da Oliveira - Serviço de Ginecologia e Obstetrícia

Guimarães

Portugal

4835-044

+351 (0)253 540 330

beatrizsilva@hospitaldeguimaraes.min-saude.pt

### Type(s)

Public

### Contact name

Dr Beatriz Bettencourt Silva

### Contact details

Rua dos Cutileiros, Creixomil  
Hospital Senhora da Oliveira - Serviço de Ginecologia e Obstetrícia  
Guimarães  
Portugal  
4835-044  
+351 (0)253 540 330  
beatrizbettsilva@gmail.com

## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

3\2019

## Study information

### Scientific Title

The role of Mifepristone on First-trimester miscarriage Treatment (MiFirsT) – a double-blind randomized controlled trial

### Acronym

MiFirsT

### Study objectives

Mifepristone followed by vaginal misoprostol is more successful at treating first-trimester miscarriage than vaginal misoprostol alone.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approved 26/02/2019, Ethics Committee for Health of Hospital Senhora da Oliveira – Guimarães (Rua dos Cutileiros, Creixomil, 4835-044 Guimarães; +351 253 540 330; comissaoetica@hospitaldeguimaraes.min-saude.pt), ref: 3\2019

### Study design

Single-center prospective interventional randomized controlled trial

### Primary study design

Interventional

### Secondary study design

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet (originally in Portuguese, attending to the study population)

**Health condition(s) or problem(s) studied**

First trimester miscarriage (embryo without cardiac activity or anembryonic gestation) up to 9 weeks of gestation, diagnosed by transvaginal ultrasonographic criteria

**Interventions**

Adult women diagnosed with first-trimester miscarriage (up to 9 weeks of gestation), who are eligible and choose medical treatment, are randomized to either treatment with oral mifepristone (200 mg) or placebo, both followed by vaginal misoprostol (800 µg).

After eligibility and written informed consent, women initiate the treatment in the Obstetrics Emergency Service of Hospital Senhora da Oliveira – Guimarães under a physician's supervision, taking orally a single-dose numbered white pill which contains either 200 mg of mifepristone (mifepristone group) or placebo (misoprostol-alone group). The pills are randomly numbered by the hospital's pharmacy in a 1:1 proportion and assigned to the participants in ascending order. Women are instructed to complete the treatment with 800 µg of vaginal misoprostol 36 to 48 hours after the oral pill and a revaluation is scheduled in 2-3 weeks at the same service. Participants and physicians involved in recruitment and follow-up are unaware of the treatment-group assignments (only the hospital pharmacy has the information about which numbered pills contained mifepristone). Vaginal misoprostol can be repeated approximately 48 hours after the first evaluation if no tissue is lost or in follow-up if missed or incomplete miscarriage is diagnosed. All patients maintain follow-up until complete miscarriage, which can take 2 months.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Mifepristone, misoprostol

**Primary outcome measure**

The success of medical treatment, defined as the complete evacuation of conception products by vaginal ultrasound and, thus, no need for surgical intervention. Treatment success is evaluated at the first follow-up appointment, 2 to 3 weeks after randomization (success rate at first follow-up) and at the second appointment, 3 to 5 weeks after randomization (success rate at second follow-up). The overall success rate and the rate of uterine aspiration/curettage is also reported.

## Secondary outcome measures

1. Complications (namely severe bleeding or pelvic infection) evaluated by the physician at follow-up appointments or admission to emergency service
2. Adverse effects (nausea, vomiting, diarrhea, headache, dizziness, chills or fever) measured by questionnaire (binomial questions) to be answered after completing the initial treatment (mifepristone or placebo plus vaginal misoprostol)
3. Intensity of bleeding and pain measured by questionnaire (Likert-type scales) to be answered after completing the initial treatment (mifepristone or placebo plus vaginal misoprostol)
4. Acceptability of the treatment measured by questionnaire (classification of the treatment as "good", "indifferent" or "bad" and if the participant would recommend it to a friend in the same clinical situation), to be answered after completing the initial treatment (mifepristone or placebo plus vaginal misoprostol)
5. Clinical characteristics that can influence treatment success (gravidity, parity, gestational age and diagnosis – embryo death or anembryonic gestation), assessed by the physician at randomization

## Overall study start date

03/12/2018

## Completion date

16/12/2021

## Eligibility

### Key inclusion criteria

1. Anembryonic or missed first-trimester miscarriage up to 9 weeks of gestation by transvaginal ultrasound (diagnosis criteria according to Society of Radiologists in Ultrasound Multispeciality Consensus Conference on Early First Trimester Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy, October 2012)
2. Healthy women aged 18 years or older

### Participant type(s)

Patient

### Age group

Adult

### Lower age limit

18 Years

### Sex

Female

### Target number of participants

Based on success rates reported by observational and interventional studies, the researchers calculate the estimated sample size of 202-256 participants with adequate power to detect a 17% difference in the rate of treatment success (73-84% in mifepristone-group; 56-67% in misoprostol-alone-group, Dunford et al., 2017, Schreiber et al., 2018), with a randomized ratio of 1:1, an overall significance level of 5% and a power of 80%.

**Total final enrolment**

216

**Key exclusion criteria**

1. Diagnosis of inevitable or incomplete miscarriage
2. Suspicious of ectopic pregnancy or trophoblastic disease
3. Intrauterine device in place
4. Allergy to prostaglandins
5. Medical conditions contraindicating the treatment with misoprostol and/or mifepristone, namely intense vaginal bleeding with severe anemia or hemodynamic instability, suspicious of systemic infection, patients with hemorrhagic disorders or on anticoagulant therapy, patients with porphyria, uncontrolled heart disease, adrenal failure or on concurrent long-term corticosteroid therapy

**Date of first enrolment**

10/04/2019

**Date of final enrolment**

25/11/2021

**Locations****Countries of recruitment**

Portugal

**Study participating centre**

**Hospital Senhora da Oliveira – Guimarães, Serviço de Ginecologia e Obstetrícia**

Rua dos Cutileiros

Creixomil

Guimarães

Portugal

4835-044

**Sponsor information****Organisation**

Hospital da Senhora da Oliveira Guimarães

**Sponsor details**

Rua dos Cutileiros

Creixomil

Guimarães

Portugal

4835-044  
+351 (0)253 540 330  
obstetricia@hospitaldeguimaraes.min-saude.pt

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.hospitaldeguimaraes.min-saude.pt/>

**ROR**

<https://ror.org/00y0jw647>

## **Funder(s)**

**Funder type**

Hospital/treatment centre

**Funder Name**

Hospital Senhora da Oliveira Guimarães

## **Results and Publications**

**Publication and dissemination plan**

Planned publication in a peer-reviewed journal. The protocol is not published or available online.

**Intention to publish date**

01/05/2023

**Individual participant data (IPD) sharing plan**

Current IPD sharing plan as of 31/07/2023:

The datasets generated during and/or analysed during the current study will be available upon request from Beatriz Bettencourt Silva (email address: [beatrizbettsilva@gmail.com](mailto:beatrizbettsilva@gmail.com)).

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**Previous IPD sharing plan:**

The participant-level data is not expected to be made available because participants gave written informed consent to store the anonymized data and to share the study results with the scientific community, not specifically to share the individual data beyond the investigation team.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>			05/01/2023	No	No
<a href="#">Basic results</a>		13/01/2023	13/01/2023	No	No