# Clinical trial results:
# Mifepristone and misoprostol versus misoprostol alone for uterine evacuation after early pregnancy failure: a pilot study

## Summary

| | |
|---|---|
| EudraCT number | 2013-001554-10 |
| Trial protocol | NL |
| Global end of trial date | 31 May 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 09 August 2022 |
| First version publication date | 09 August 2022 |
| Summary attachment (see zip file) | Pilot study article (M&M pilot study.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | NL57892 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Radboudumc |
| Sponsor organisation address | Geert Grooteplein-Zuid 10, Nijmegen, Netherlands, 6525GA |
| Public contact | Afdeling Gynaecologie, Radboudumc, +31 0243614788, menm.trial@gmail.com |
| Scientific contact | Afdeling Gynaecologie, Radboudumc, +31 0243614788, menm.trial@gmail.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 | 01 September 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 May 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This study will compare sequential mifepristone and misoprostol ("M&M") treatment versus misoprostol treatment alone, which is currently the standard medical treatment in the Netherlands.

Protection of trial subjects:

Ethics approval was obtained; CMO Arnhem-Nijmegen, file number 2015-2264, NL 57892.091.16.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 October 2016 |
| 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: 40 |
| Worldwide total number of subjects | 40 |
| EEA total number of subjects | 40 |

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) | 40 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A two-centred, prospective, two-armed, randomized, double blinded and placebo-controlled pilot trial was performed, situated in an academic (Radboud University Medical Centre) and a teaching hospital (Canisius-Wilhelmina Hospital) in Nijmegen, the Netherlands, between October 2016 and May 2017.

### Pre-assignment

Screening details:

Woman with a diagnosis of EPF between 6 and 14 weeks of gestation were eligible, defined by transvaginal ultrasonography as an intra-uterine pregnancy and a crown-rump length ≥ 6 mm and no cardiac activity, or a gestational sac without embryonic pole confirmed by a second ultrasound at least one week later.

### Period 1

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

Blinding implementation details:

The blinding of patients and physicians for treatment arm was maintained until the follow-up (questionnaire four weeks after treatment) of the last included patient was completed

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | M&M group |

Arm description:

Mifepristone + misoprostol

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | mifepristone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

200mg oral once

| | |
|---|---|
| **Arm title** | placebo |

Arm description:

placebo + misoprostol

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

Dosage and administration details:

placebo, once

| **Number of subjects in period 1** | M&M group | placebo |
|---|---|---|
| Started | 20 | 20 |
| Completed | 20 | 20 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | M&M group |
| Reporting group description: Mifepristone + misoprostol | |
| Reporting group title | placebo |
| Reporting group description: placebo + misoprostol | |

| Reporting group values | M&M group | placebo | Total |
|---|---|---|---|
| Number of subjects | 20 | 20 | 40 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 20 | 20 | 40 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 20 | 20 | 40 |
| Male | 0 | 0 | 0 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | M&M |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Data were analysed according to intention to treat method. The main outcome variable was complete evacuation after medical treatment and was assessed by calculating success rates, relative risks and 95% confident intervals in both groups. To evaluate the potential of each of the strategies, we also performed a per protocol analysis, taking into account only those cases that were treated according to protocol.

SPSS version 24 was used for data analysis. Differences between groups were analysed using the Pearson’s chi-square test or the Fisher’s exact test for categorical variables. Mann-Whitney U test was used for non-normally distributed metric variables. Logistic regression analysis was performed to identify factors that were associated with treatment success. P-values smaller than 0.05, were considered significant.

| Reporting group values | M&M | | |
|---|---|---|---|
| Number of subjects | 39 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 39 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 39 | | |
| Male | 0 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | M&M group |
| Reporting group description: Mifepristone + misoprostol | |
| Reporting group title | placebo |
| Reporting group description: placebo + misoprostol | |
| Subject analysis set title | M&M |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Data were analysed according to intention to treat method. The main outcome variable was complete evacuation after medical treatment and was assessed by calculating success rates, relative risks and 95% confident intervals in both groups. To evaluate the potential of each of the strategies, we also performed a per protocol analysis, taking into account only those cases that were treated according to protocol.

SPSS version 24 was used for data analysis. Differences between groups were analysed using the Pearson's chi-square test or the Fisher's exact test for categorical variables. Mann-Whitney U test was used for non-normally distributed metric variables. Logistic regression analysis was performed to identify factors that were associated with treatment success. P-values smaller than 0.05, were considered significant.

### Primary: Complete evacuation

| | |
|---|---|
| End point title | Complete evacuation |

End point description:

Primary and secondary outcome measures were extracted from the patient medical record, diary, digital questionnaires and/or case report form. The primary outcome parameter, complete (success) or incomplete (failure) evacuation, was determined by transvaginal ultrasonography one week (six to nine days) after medical treatment. Expulsion of the gestational sac and an endometrial thickness < 15 mm (maximum anterior-posterior diameter) using only the allocated therapy by randomization was considered as complete evacuation.[7, 9, 18-20] D&C performed because of heavy vaginal bleeding during medical treatment was also considered as failure.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

follow up untill 6 weeks after medical treatment

| End point values | M&M group | placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 19 | | |
| Units: ultrasonography / clinical assessment | | | | |
| number (not applicable) | 20 | 19 | | |

### Statistical analyses

| **Statistical analysis title** | complete evacuation |
|---|---|
| Comparison groups | placebo v M&M group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANOVA |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| 6 weeks after medical treatment | |
| Adverse event reporting additional description: | |
| adverse events were reported in either group. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | test |
| Dictionary version | 2 |

| Reporting groups | |
|---|---|
| Reporting group title | both |
| Reporting group description: | |
| No serious adverse events were reported in either group. Quality of life was similar in both groups. | |

| Serious adverse events | both | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | both | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | | |
| Surgical and medical procedures | | | |
| curettage | Additional description: The need for D&C was significantly lower in the M&M group as compared to the placebo group: 2/19 (10,5%) versus 10/20 (50%) respectively (p 0.008, RR 1.789, 95% CI 1.124-2.848). | | |
| subjects affected / exposed | 3 / 40 (7.50%) | | |
| occurrences (all) | 3 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported