



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 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 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			
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			
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