Clinical trial results:
Pre-treatment with Mifepristone prior to Mirena insertion for optimizing bleeding pattern in pre-menopausal women

Summary

EudraCT number	2009-009014-40
Trial protocol	SE
Global end of trial date	30 January 2015

Results information

Result version number	v1 (current)
This version publication date	31 March 2021
First version publication date	31 March 2021

Trial information

Trial identification

Sponsor protocol code	W2009M

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01931657
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	17177, Stockholm, Sweden,
Public contact	Kristina Gemzell Danielsson, Karolinska Institutet, kristina.gemzell@ki.se
Scientific contact	Kristina Gemzell Danielsson, Karolinska Institutet, kristina.gemzell@ki.se

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	30 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2015
Global end of trial reached?	Yes
Global end of trial date	30 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the present study is to study in pre-menopausal women requesting Mirena for contraception:
1. the effect of pre-treatment with mifepristone on the bleeding pattern in women using the Mirena contraceptive system

Protection of trial subjects:

Follow-up was done with visits to the clinic monthly for the first 3 months, at 6 months post LNGIUS insertion and with a telephone contact at the 12 months end-of-trial evaluation. Also, a transvaginal ultrasound examination was performed at baseline, prior to LNG-IUS insertion and then monthly for 3 months after the LNG-IUS insertion as well as at 6 months after insertion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2009
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	Sweden: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	58

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a prospective, randomized, double blind, placebo-controlled trial to evaluate the effect of pre-treatment with a low dose mifepristone on bleeding pattern in women requesting LNG-IUS 52 mg as a contraceptive method. The study was conducted at the Karolinska University Hospital from November 2009 to January 2015.

Pre-assignment

Screening details:

Screening criteria: healthy women, opting for LNG-IUS 52 mg for contraception, aged 18–43 with regular and normal menstrual cycles lasting 24–35 days, with no contraindications to LNG-IUS or mifepristone.

Period 1

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

Blinding implementation details:

Women received mifepristone (Mifegyne®, Exelgyn, Paris, France) or visually indistinguishable vitamin B (TrioBe® Recip, Stockholm, Sweden). The tablets were divided by the study nurse.

Arms

Are arms mutually exclusive?	Yes
Arm title	Mifepristone

Arm description:

50 mg mifepristone) was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.

Arm type	Experimental
Investigational medicinal product name	Mifepristone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.

Arm title	Placebo

Arm description:

Women in placebo received visually indistinguishable vitamin B (TrioBe® Recip, Stockholm, Sweden) and was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.

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

Dosage and administration details:

One quarter of the comparator (TrioB) was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.

Number of subjects in period 1	Mifepristone	Placebo
Started	29	29
Completed	26	23
Not completed	3	6
Consent withdrawn by subject	3	3
Pregnancy	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Mifepristone
Reporting group description:	
50 mg mifepristone) was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.	
Reporting group title	Placebo
Reporting group description:	
Women in placebo received visually indistinguishable vitamin B (TrioBe® Recip, Stockholm, Sweden) and was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.	

Reporting group values	Mifepristone	Placebo	Total
Number of subjects	29	29	58
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	31	27	
full range (min-max)	20 to 41	20 to 43	-
Gender categorical			
Units: Subjects			
Female	29	29	58
Male	0	0	0
Pregnancies			
Units: Number			
median	1.5	1	
full range (min-max)	0 to 5	0 to 5	-
Parity			
Units: Number			
median	0	0	
full range (min-max)	0 to 3	0 to 4	-
Cycle lengths			
Units: Days			
median	29	28	
full range (min-max)	27 to 32	24 to 35	-

Duration of menstrual period Units: Days			
median	5	5	
full range (min-max)	3 to 7	3 to 7	-
BMI Units: BMI			
median	22.9	23.8	
full range (min-max)	18.2 to 30.4	18.4 to 32.0	-

End points

End points reporting groups

Reporting group title	Mifepristone
Reporting group description:	
50 mg mifepristone) was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.	
Reporting group title	Placebo
Reporting group description:	
Women in placebo received visually indistinguishable vitamin B (TrioBe® Recip, Stockholm, Sweden) and was to be taken orally every other day starting on the first day of the menstrual cycle for the pre-treatment period. The pre-treatment period was 2 months (corresponding to two menstrual cycles i.e. 2 × 28 days) prior to insertion and until 3 days (±2 days) following the LNG-IUS insertion.	

Primary: Bleeding pattern in women after insertion of the LNG-IUS

End point title	Bleeding pattern in women after insertion of the LNG-IUS
End point description:	
End point type	Primary
End point timeframe:	
3 months after insertion of the LNG-IUS.	

End point values	Mifepristone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: % days with bleeding and spotting	40	38		

Statistical analyses

Statistical analysis title	Difference in bleeding patterns
Statistical analysis description:	
Difference in percentage days with bleeding and spotting 3 months following insertion of the LNG-IUS.	
Comparison groups	Mifepristone v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.838
Method	Mann-Whitney U-test
Parameter estimate	Median difference (final values)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From pre-treatment with Mifepristone and up to 12 months after insertion of LNG-IUS.

Assessment type	Systematic

Dictionary used

Dictionary name	ICD
Dictionary version	10

Reporting groups

Reporting group title	Mifepristone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Mifepristone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Mifepristone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no side effects or non-serious adverse events related to the study treatment, other than bleeding. But bleeding was a main outcome, so it was not counted as an adverse event.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Limitations of the study include its small sample size, and the fact that the observed difference in bleeding and spotting days between study groups was small and short lasting.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30295731