# 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<br>Units: Days | | | |
| median | 5 | 5 | |
| full range (min-max) | 3 to 7 | 3 to 7 | - |
| BMI<br>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