# Clinical trial results:
# Usefulness of medroxyprogesterone acetate in the follicular phase for ovarian donors to prevent premature luteinization

## Summary

| | |
|---|---|
| EudraCT number | 2017-002341-30 |
| Trial protocol | ES |
| Global end of trial date | 25 June 2019 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 February 2022 |
| First version publication date | 02 February 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 1705-VLC-030-JG |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03300960 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | IVI VALENCIA |
| Sponsor organisation address | plaza policia local, valencia, Spain, 46015 |
| Public contact | Juan Giles, INSTITUTO VALENCIANO DE INFERTILIDAD (IVI), +34 963050900, juan.giles@ivi.es |
| Scientific contact | Juan Giles, INSTITUTO VALENCIANO DE INFERTILIDAD (IVI), +34 963050900, juan.giles@ivi.es |

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 | 14 January 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 October 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 June 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To compare the number of oocytes and metaphase II oocytes (MII) from donors that have received ovarian stimulation with FSHr and in which it has been used to an antagonist of GnRH vs AMP for prevent early luteinization.

Protection of trial subjects:

Not applicable.

Background therapy:

Decapeptyl and Bemfola were uses as background treatment involved on the controlled ovarian stimulation proccedure used in both treatment arms. Both treatments were considered as routine clinical practice.

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 11 September 2017 |
| 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 | Spain: 318 |
| Worldwide total number of subjects | 318 |
| EEA total number of subjects | 318 |

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) | 318 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

318 healthy women has been recruited.
First Patient First Visit:20 oct 2017
Last Patient Last Visit: 25 jun 2019

### Pre-assignment

Screening details:

327 healthy women has been selected to participate.
318 were Randomized (161 Treatmen group- 156 Control group)
Data from 308 were Analized (157 Treatmen group- 151 Control group)

### Period 1

| | |
|---|---|
| Period 1 title | Overal trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Experimental (Provera) |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Medroxyprogesterone acetate |
| Investigational medicinal product code | SUB03114MIG |
| Other name | |
| Pharmaceutical forms | Buccal tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One 10 mg tablet of MPA (Medroxyprogesterone acetate) is administered every 24 hours from the onset of Controlled Ovarian Stimulation (COS), until the day of triggering.

| | |
|---|---|
| **Arm title** | ACTIVE COMPARATOR |

Arm description: -

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | GANIRELIX |
| Investigational medicinal product code | SUB07883MIG |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.25 mg of Ganirelix (GnRH antagonist) a day once diameter of follicles are 14 mm diameter on average until triggering.

| **Number of subjects in period 1** | Experimental (Provera) | ACTIVE COMPARATOR |
|---|---|---|
| Started | 161 | 157 |
| Completed | 157 | 151 |
| Not completed | 4 | 6 |
| Consent withdrawn by subject | - | 1 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 1 | 1 |
| Lack of efficacy | 2 | 2 |
| Protocol deviation | 1 | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overal trial |

Reporting group description: -

| Reporting group values | Overal trial | Total | |
|---|---|---|---|
| Number of subjects | 318 | 318 | |
| 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 24.19 | | |
| standard deviation | ± 4.43 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 318 | 318 | |
| Male | 0 | 0 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Experimental (Provera) |
| Reporting group description: - | |
| Reporting group title | ACTIVE COMPARATOR |
| Reporting group description: - | |

### Primary: number of oocytes obtained

| | |
|---|---|
| End point title | number of oocytes obtained |
| End point description: | |
| Compare the number of oocytes and metaphase II (MII) oocytes from donors who have undergone ovarian stimulation with FSHr, in whom GnRH antagonist vs. MPA was employed to prevent early luteinization | |
| End point type | Primary |
| End point timeframe: | |
| 10 days after COS (Controlled ovarian stimulation) | |

| End point values | Experimental (Provera) | ACTIVE COMPARATOR | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 161 | 157 | | |
| Units: oocytes | 21 | 21 | | |

### Statistical analyses

| Statistical analysis title | Non inferiority analysis |
|---|---|
| Comparison groups | Experimental (Provera) v ACTIVE COMPARATOR |
| Number of subjects included in analysis | 318 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.949 |
| Method | t-test, 1-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.233 |
| upper limit | 2.517 |

## Primary: Metaphase II (MII) oocytes

| | |
|---|---|
| End point title | Metaphase II (MII) oocytes |
| End point description: | |

| | |
|---|---|
| End point type | Primary |
| End point timeframe: | |
| overall study | |

| End point values | Experimental (Provera) | ACTIVE COMPARATOR | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 161 | 156 | | |
| Units: number of oocytes | 16 | 16 | | |

## Statistical analyses

| Statistical analysis title | Metaphase II Oocytes |
|---|---|
| Statistical analysis description: | |
| Number of Metaphase II Oocytes obtained | |
| Comparison groups | ACTIVE COMPARATOR v Experimental (Provera) |
| Number of subjects included in analysis | 317 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.802 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.068 |
| upper limit | 1.712 |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

30 days

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Experimental (Provera) |

Reporting group description:

Oocyte donor women aged between 18 and 35 years with normal ovarian function and who will follow ovarian stimulation in cycle with rFSH combined with medroxyprogesterone acetate in the follicular phase as a preventive of early luteinisation.

| | |
|---|---|
| Reporting group title | ACTIVE COMPARATOR |

Reporting group description:

Oocyte donor women aged between 18 and 35 years with normal ovarian function and who will follow ovarian stimulation in cycle with rFSH combined with GnRH antagonists.

| Serious adverse events | Experimental (Provera) | ACTIVE COMPARATOR | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 156 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | Additional description: ABDOMINAL PAIN IN THE RIGHT ILIAC FOSSA REQUIRING HOSPITALISATION | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 156 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Experimental (Provera) | ACTIVE COMPARATOR | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 71 / 161 (44.10%) | 68 / 156 (43.59%) | |
| General disorders and administration site conditions | | | |
| Abdominal pain lower | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 71 / 161 (44.10%)<br>71 | 68 / 156 (43.59%)<br>68 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 08 November 2018 | some changes related to folliculometry adjusted to standard clinical practice and to the inclusion visit in the case of participants taking OCPs, in order to avoid protocol deviations.<br><br>he protocol indicates that the GnRH antagonist will be administered from the time 14 mm mean diameter is reached, but in routine clinical practice, it can be started on the 6th day of stimulation at the investigator's discretion even if there are no 14 mm follicles. This change is included in order to avoid deviations from the protocol.<br>A modification is made in relation to the number of follicles with an adequate diameter for ovulation induction with the administration of the triptorelin bolus; in standard clinical practice, at least 8 follicles with an average size greater than 14 mm are required and at least 2-3 must reach an average diameter of ≥ 17 mm in order to induce ovulation. This correction is made with respect to the minimum number of follicles in order to avoid deviations from the protocol.<br>A correction is made regarding the inclusion visit when the donor is taking OCPs. The approved protocol indicates that the participant will first make visit 0 and sign the IC, undergo procedures and then attend visit 1a, where they will be randomised. A correction is made in which the donor can come directly to the clinic at visit 1A where she will sign the IC, if she is on the 5th day of the end of OCPs, as this is the usual practice in the clinic.<br>The intention to compensate participants for any inconvenience caused is included in the protocol.<br>The new version updates the data on the duration of the study and corrects the initial error in relation to the dates provided in the calendar.<br><br>Translated with www.DeepL.com/Translator (free version) |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported