



## 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
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##### 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
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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 Treatment group- 156 Control group)

Data from 308 were Analyzed (157 Treatment group- 151 Control group)

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	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.

<b>Arm title</b>	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.

<b>Number of subjects in period 1</b>	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	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	318	318	
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			
arithmetic mean	24.19		
standard deviation	± 4.43	-	
Gender categorical			
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
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End point description:

End point type	Primary
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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
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Statistical analysis description:

Number of Metaphase II Oocytes obtained

Comparison groups	ACTIVE COMPARATOR v Experimental (Provera)
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Number of subjects included in analysis	317
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Analysis specification	Pre-specified
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Analysis type	non-inferiority
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P-value	< 0.802
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Method	t-test, 2-sided
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Parameter estimate	Mean difference (final values)
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-2.068
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upper limit	1.712
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## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

30 days

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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### Reporting groups

Reporting group title	Experimental (Provera)
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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
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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	71 / 161 (44.10%)	68 / 156 (43.59%)	
occurrences (all)	71	68	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 November 2018	<p>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.</p> <p>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.</p> <p>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 <math>\geq 17</math> 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.</p> <p>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.</p> <p>The intention to compensate participants for any inconvenience caused is included in the protocol.</p> <p>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.</p> <p>Translated with <a href="http://www.DeepL.com/Translator">www.DeepL.com/Translator</a> (free version)</p>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported