Clinical trial results:
Scheduling of GnRH antagonist FIV-ICSI cycles with estrogen or contraceptive oral pills in previous luteal phase. Comparison of results against no treatment.

Summary

EudraCT number	2014-001809-40
Trial protocol	ES
Global end of trial date	23 July 2018

Results information

Result version number	v1 (current)
This version publication date	01 January 2025
First version publication date	01 January 2025
Summary attachment (see zip file)	Final results (INFORME FINAL DE RESULTADOS.pdf)

Trial information

Trial identification

Sponsor protocol code	MER001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	IDIPAZ
Sponsor organisation address	Paseo castellana 261, MADRID, Spain,
Public contact	Sara Fernández Prada, Sara Fernández Prada Servicio de Reproducción Humana del Hospital la Paz, +34 606823685,
Scientific contact	Sara Fernández Prada, Sara Fernández Prada Servicio de Reproducción Humana del Hospital la Paz, 0034 606823685,

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 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 July 2018
Global end of trial reached?	Yes
Global end of trial date	23 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Comparing gestational outcomes like pregnancy rate, clinical pregnancy rate, miscarriage rate or live birth rate between patients pretreated with estrogen pills, contraceptive pills and no pretreated .

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2015
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: 106
Worldwide total number of subjects	106
EEA total number of subjects	106

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)	106
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is a prospective longitudinal interventional study in 3 cohorts in which we will compare patients undergoing IVF-ICSI treatment in protocol with
compare patients undergoing IVF-ICSI treatment in protocol with antagonists who meet the inclusion and exclusion

Pre-assignment

Screening details:

patients randomized into three groups, group 1 pretreated with estradiol valerate, group 2 pretreated with oral contraceptives, group 3, no hormonal treatment in previous luteal phase

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	arm 1

Arm description:

preconceptive treatment

Arm type	Active comparator
Investigational medicinal product name	levonorgestrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

oral contraceptive treatment arm (levonorgestrel 150 mcg/ ethinylestradiol 0.3 mcg) will start treatment on the 1st-2nd day of menstruation of the previous cycle for at least 12 days, with 5 days of washout thereafter, after which controlled ovarian stimulation will be initiated.

Arm title	arm 2

Arm description:

oestradiol valerate

Arm type	Active comparator
Investigational medicinal product name	oestradiol valerate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

treatment arm will start treatment 3 days before their expected period with a dose of 2 mg/12 hours until the day before the start of ovarian stimulation, which will begin between the 2nd-8th day of the cycle.

Arm title	arm 3

Arm description:

no preatreatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	arm 1	arm 2	arm 3
Started	39	32	35
Completed	34	25	27
Not completed	5	7	8
medication incompatibilities	-	-	5
Pregnancy	-	1	1
poor adherence	2	4	-
Lost to follow-up	-	1	2
patient decision	3	1	-

Baseline characteristics

Reporting groups	
Reporting group title	period 1

Reporting group description: -

Reporting group values	period 1	Total	
Number of subjects	106	106	
Age categorical			
18-40 years			
Units: Subjects			
18-40		0	
Age continuous			
18-40 years			
Units: years			
median	35.35		
full range (min-max)	28 to 40	-	
Gender categorical			
Units: Subjects			
Female	106	106	
Male	0	0	

End points

End points reporting groups

Reporting group title	arm 1
Reporting group description: preconceptive treatment	
Reporting group title	arm 2
Reporting group description: oestradiol valerate	
Reporting group title	arm 3
Reporting group description: no preatreatment	

Primary: EVALUATE GESTATIONAL OUTCOMES

End point title	EVALUATE GESTATIONAL OUTCOMES

End point description:

To evaluate the gestational outcomes (clinical gestation rate, miscarriage and live birth) obtained in patients with a normo-responder profile, undergoing IVF-ICSI treatment in an antagonist protocol with pre-treatment in previous luteal phase (oestradiol valerate or combined oral contraceptives) versus the outcomes observed in patients without previous pre-treatment.

End point type	Primary

End point timeframe:

during the study period

End point values	arm 1	arm 2	arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	25	27	
Units: %	34	25	27	

Statistical analyses

Statistical analysis title	Mean exposure time
Comparison groups	arm 3 v arm 1 v arm 2
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.078
Method	SD
Parameter estimate	standard deviation

Statistical analysis title	Mean exposure time

Comparison groups	arm 2 v arm 1 v arm 3
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.941
Method	SD

Statistical analysis title	no pretreatment
Comparison groups	arm 1 v arm 2 v arm 3
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0 [2]
Method	SD

Notes:

[1] - NO AVAILABLE

[2] - NOT AVAILABLE

Secondary: To evaluate the number of ovarian follicles observed ultrasonographically at the end of the stimulation, the number of oocytes obtained, the oocyte maturity rate and the number of embryos evolved in the different study groups.

End point title	To evaluate the number of ovarian follicles observed ultrasonographically at the end of the stimulation, the number of oocytes obtained, the oocyte maturity rate and the number of embryos evolved in the different study groups.

End point description:

End point type	Secondary

End point timeframe:

during the hole study

End point values	arm 1	arm 2	arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	25	27	
Units: number	34	25	27	

Statistical analyses

Statistical analysis title	number of follicles SD

Statistical analysis description:

NUMBER OF FOLLICLES > 16 mm on the day of the ovulatory trigger.

Comparison groups	arm 1 v arm 2 v arm 3

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.564
Method	SD

Secondary: To evaluate the possible association of the exposure time to the different pretreatments with the reproductive results.

End point title	To evaluate the possible association of the exposure time to the different pretreatments with the reproductive results.

End point description:

End point type	Secondary

End point timeframe:

during the hole study

End point values	arm 1	arm 2	arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	25	27	
Units: days	34	25	27	

Statistical analyses

Statistical analysis title	GROUP PRETREATED WITH CONTRACEPTIVES
Comparison groups	arm 1 v arm 2
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.941
Method	SD

Statistical analysis title	GROUP PRETREATED WITH OESTROGENS
Comparison groups	arm 2 v arm 1
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.078
Method	SD

Secondary: To assess the cancellation rate due to insufficient response or absence of viable embryos observed in the different study groups.

End point title	To assess the cancellation rate due to insufficient response or absence of viable embryos observed in the different study groups.

End point description:

End point type	Secondary

End point timeframe:

during the hole study

End point values	arm 1	arm 2	arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	25	27	
Units: %	34	25	27	

Statistical analyses

Statistical analysis title	cycle cancellation rate
Comparison groups	arm 1 v arm 2 v arm 3
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.307
Method	SD

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

during the hole study

Adverse event reporting additional description:

No clinically relevant alterations were found in phisical examination or vital signs. No side effects were reported.
No adverse events were detected in the patients included in the study. There were no deaths, other serious adverse events or other significant adverse events during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Frequency threshold for reporting non-serious adverse events: 0 %

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: NO adverse events found

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