Clinical trial results:
Analysis of follicular steroid synthesis during controlled ovarian stimulation with recombinant FSH vs HMG in GnRH antagonist cycles

Summary

EudraCT number	2015-005762-28
Trial protocol	ES
Global end of trial date	15 June 2018

Results information

Result version number	v1 (current)
This version publication date	14 November 2021
First version publication date	14 November 2021
Summary attachment (see zip file)	1512-VLC-066-EB-RESULTS (RESULTS 1512-VLC-066-EB.pdf)

Trial information

Trial identification

Sponsor protocol code	1512-VLC-066-EB

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02738580
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IVI
Sponsor organisation address	PLAZA POLICIA LOCAL 1, VALENCIA, Spain,
Public contact	Ernesto Bosch, IVI Valencia, Ernesto.Bosch@ivirma.com
Scientific contact	Ernesto Bosch, IVI Valencia, Ernesto.Bosch@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	15 June 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare serum concentrations of the different hormones involved in follicular steroid genesis during a cycle of controlled ovarian stimulation with recombinant FSH or HMG

Protection of trial subjects:

Not aplicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2016
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: 112
Worldwide total number of subjects	112
EEA total number of subjects	112

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)	112
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

114 were evaluated for selecction. 112 patient were included. 104 patients were completed.

Pre-assignment

Screening details:

112 were evaluated for selecction.
56 were randomized to hpHMG group:
- Cycle Cancelled due to low response: 2
- Voluntary withdrawal from trial: 1
- Excluded from the donation programme: 1

56 were randomized to rFSH
- Cycle cancelled due to low response: 3
- Cycle cancelled due to SAE: 1

104 patients were completed.

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	rFSH

Arm description:

Oocyte donor with normal ovarian function, who will follow ovarian stimulation in cycle with GnRH Antagonists and rFSH.

Arm type	Experimental
Investigational medicinal product name	recombinant FSH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

as usual clinical practice

Arm title	HP-hmg

Arm description:

Oocyte donor with normal ovarian function, who will follow ovarian stimulation in cycle with GnRH Antagonists and HP-HMG.

Arm type	Active comparator
Investigational medicinal product name	HP-HMG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

AS CLINICAL PRACTICE

Number of subjects in period 1	rFSH	HP-hmg
Started	56	56
Completed	52	52
Not completed	4	4
Adverse event, non-fatal	1	-
WITHDRAWAL CONSENT	-	1
EXCLUDED FROM DONNOR PROGRAM	-	1
Lack of efficacy	3	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	rFSH

Reporting group description:

Oocyte donor with normal ovarian function, who will follow ovarian stimulation in cycle with GnRH Antagonists and rFSH.

Reporting group title	HP-hmg

Reporting group description:

Oocyte donor with normal ovarian function, who will follow ovarian stimulation in cycle with GnRH Antagonists and HP-HMG.

Primary: SERUM PROGESTERONE CONCENTRATION

End point title	SERUM PROGESTERONE CONCENTRATION

End point description:

COMPARE HORMONAL BLOOD SERUM CONCENTRATIONS OF PROGESTERONE DURING OVARIAN STIMULATION IMPLIED IN FOLLICULAR STEROIDOGENESIS DURING A CYCLE OF CONTROLLED OVARIAN STIMULATION WITH EITHER r-FSH OR HP-HMG

End point type	Primary

End point timeframe:

overal study

End point values	rFSH	HP-hmg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: ng/mL				
arithmetic mean (confidence interval 95%)	0.74 (0.22 to 1.26)	0.45 (0.19 to 0.71)		

Statistical analyses

Statistical analysis title	SERUM PROGESTERONE LEVELS
Comparison groups	rFSH v HP-hmg
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Median difference (final values)
Point estimate	0.29

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	1.26
Variability estimate	Standard deviation
Dispersion value	0.26

Notes:

[1] - THE PROPORTION OF PATIENTS WITH ELEVATED PROGESTERONE ON LAST DAY OF STIMULATION WAS COMPARED BETWEEN BORTH GROUPS USING THE CHI-SQUERE TEST

Primary: OVARIAN RESPONSE

End point title	OVARIAN RESPONSE

End point description:

NUMBER OF FOLICLES REACHED AND PUNCTURED AFTER CONTROLED OVARIAN STIMULATION

End point type	Primary

End point timeframe:

OVERAL STUDY

End point values	rFSH	HP-hmg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: NUMBER OF FOLICLES				
number (confidence interval 95%)	16.5 (9 to 24)	17.5 (9.6 to 25.4)		

Statistical analyses

Statistical analysis title	OVARIAN RESPONSE

Statistical analysis description:

NUMBER OF FOLICLES REACHED AND PUNCTURED AFTER CONTROLED OVARIAN STIMULATION

Comparison groups	rFSH v HP-hmg
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.49
Method	t-test, 1-sided

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

21 DAYS

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	r-FSH

Reporting group description: -

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 AE has been reported.

Serious adverse events	r-FSH		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 52 (1.92%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Coagulation test abnormal	Additional description: VITAMIN K DEFICIENCY SHOWED AS COAGULATION PANEL ALTERATON. PT: 15,4 seg; INR: 1,3; Quick Index: 69%; TTPA: 38 seg. Hemmatic parameters at minimum normal limits She was reffered to hemathologist department. There was not more information about		
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	r-FSH		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)		

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