



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 applicable.

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 selection. 112 patients were included. 104 patients were completed.

Pre-assignment

Screening details:

112 were evaluated for selection.

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: overall 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 FOLLICLES REACHED AND PUNCTURED AFTER CONTROLLED 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 FOLLICLES | | | | |
| 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 FOLLICLES REACHED AND PUNCTURED AFTER CONTROLLED 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 ALTERATION. PT: 15,4 seg; INR: 1,3; Quick Index: 69%; TTPA: 38 seg. Hemmatic parameters at minimum normal limits She was referred 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