



Clinical trial results:

CLINICAL TRIAL, SINGLE BLIND, RANDOMIZED, CONTROLLED PROSPECTIVE EVALUATION FOR OPTIMUM TIME INTERVAL BETWEEN ACETATE ADMINISTRATION AND PUNCTURE TRIPTORELIN FOLLICULAR IN IVF TREATMENT

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2012-005571-14 |
| Trial protocol | ES |
| Global end of trial date | 02 February 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 12 February 2022 |
| First version publication date | 12 February 2022 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | TIMING |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02244151 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Instituto de Investigación Sanitaria La Fe de Valencia |
| Sponsor organisation address | Avenida Fernando Abril Martorell, Torre 106 A 7planta, 46026 València, , Valencia, Spain, |
| Public contact | UICEC , INSTITUTO DE INVESTIGACION SANITARIA LA FE, 34 961246611, investigacion_clinica@iislafe.es |
| Scientific contact | UICEC, INSTITUTO DE INVESTIGACION SANITARIA LA FE, 34 961246611, investigacion_clinica@iislafe.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 | 02 February 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 February 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 February 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Identify the optimal time interval between administration of the GnRH analogue triptorelin acetate and needle aspiration of oocytes

Protection of trial subjects:

The reference study was conducted in Spain under the legal framework of Royal Decree 1090/2015. It has been performed in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, adopted by the General Assembly of the World Medical Association (1996). In addition, the study has been conducted in accordance with the protocol, good clinical practice (GCP) in accordance with the guidelines of the international conference on harmonization (ICH) and regulatory requirements for participating institutions.

An appropriately performed informed consent has been used, in compliance with GCP according to ICH guidelines and approved by the CEIm of the Hospital Universitario y Politécnico La Fe. Prior to inclusion of subjects in the study, a copy of the CEIm-approved informed consent has been reviewed with the prospective participant, signed and dated. The investigator has provided a copy of each subject's signed informed consent form and has retained a copy in the subject's study file.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 01 August 2013 |
| 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: 152 |
| Worldwide total number of subjects | 152 |
| EEA total number of subjects | 152 |

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) | 152 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The recruitment started on 08 September 2014, and ended on 2 February 2018. A number of 131 patients were included, 127 patients completed all the study procedures and 4 patients were excluded.

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 152 |
| Number of subjects completed | 131 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|------------------------|
| Reason: Number of subjects | Protocol deviation: 21 |
|----------------------------|------------------------|

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Investigator ^[1] |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|----------------|
| Arm title | 30 hours Group |
|------------------|----------------|

Arm description:

Follicular puncture 30 hours after administration of Decapeptyl®.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | DECAPEPTYL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solvent for solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous route. Dose: 0.2 mg single dose.

| | |
|------------------|----------------|
| Arm title | 36 hours Group |
|------------------|----------------|

Arm description:

control

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | DECAPEPTYL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solvent for solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous route. Dose: 0.2 mg single dose.

| | |
|------------------|----------------|
| Arm title | 40 hours group |
|------------------|----------------|

Arm description:

Follicular puncture 40 hours after administration of Decapeptyl®.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | DECAPEPTYL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solvent for solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subcutaneous route. Dose: 0.2 mg single dose.

| | |
|------------------|--------------|
| Arm title | Not recorded |
|------------------|--------------|

Arm description: -

| | |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Given the characteristics of the trial and the treatment, only the collaborating team was the one who did not know how long it was necessary to wait for the treatment until the time of making the puncture.

| Number of subjects in period 1^[2] | 30 hours Group | 36 hours Group | 40 hours group |
|---|----------------|----------------|----------------|
| Started | 42 | 43 | 41 |
| Completed | 40 | 43 | 40 |
| Not completed | 2 | 0 | 1 |
| Consent withdrawn by subject | - | - | 1 |
| Protocol deviation | 2 | - | - |

| Number of subjects in period 1^[2] | Not recorded |
|---|--------------|
| Started | 5 |
| Completed | 5 |
| Not completed | 0 |
| Consent withdrawn by subject | - |
| Protocol deviation | - |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 152 patients were preselected, of which 131 were randomized, giving rise to the different groups and numbers of patients.

Baseline characteristics

Reporting groups

| | |
|---|----------------|
| Reporting group title | 30 hours Group |
| Reporting group description: Follicular puncture 30 hours after administration of Decapeptyl®. | |
| Reporting group title | 36 hours Group |
| Reporting group description: control | |
| Reporting group title | 40 hours group |
| Reporting group description: Follicular puncture 40 hours after administration of Decapeptyl®. | |
| Reporting group title | Not recorded |
| Reporting group description: - | |

| Reporting group values | 30 hours Group | 36 hours Group | 40 hours group |
|---------------------------------------|----------------|----------------|----------------|
| Number of subjects | 42 | 43 | 41 |
| Age categorical Units: Subjects | | | |
| 18 - 37 | 42 | 43 | 41 |
| Gender categorical Units: Subjects | | | |
| Female | 42 | 43 | 41 |

| Reporting group values | Not recorded | Total | |
|---------------------------------------|--------------|-------|--|
| Number of subjects | 5 | 131 | |
| Age categorical Units: Subjects | | | |
| 18 - 37 | 5 | 131 | |
| Gender categorical Units: Subjects | | | |
| Female | 5 | 131 | |

End points

End points reporting groups

| | |
|---|----------------|
| Reporting group title | 30 hours Group |
| Reporting group description: Follicular puncture 30 hours after administration of Decapeptyl®. | |
| Reporting group title | 36 hours Group |
| Reporting group description: control | |
| Reporting group title | 40 hours group |
| Reporting group description: Follicular puncture 40 hours after administration of Decapeptyl®. | |
| Reporting group title | Not recorded |
| Reporting group description: - | |

Primary: ovarian stimulation cycle

| | |
|---|--|
| End point title | ovarian stimulation cycle ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: To determine the optimal time interval between the administration of the GnRH analog triptorelin acetate (Decapeptyl®) and the puncture-aspiration of oocytes in IVF treatments, evaluating the difference obtained in the number of mature oocytes obtained. | |

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The research team decided that there was no significance in the 24h group, so no data was collected from it.

| End point values | 30 hours Group | 36 hours Group | 40 hours group | |
|---|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 40 | 43 | 40 | |
| Units: media | | | | |
| median (standard deviation) | | | | |
| Stimulation duration (days) | 9.85 (± 1.51) | 10.19 (± 1.47) | 10.40 (± 1.75) | |
| Initial dose FSH (mcg) | 132.89 (± 24.04) | 138.10 (± 21.55) | 132.50 (± 24.15) | |
| Total additional rFSH dose (IU) | 708.55 (± 440.76) | 839.88 (± 578.53) | 797.50 (± 513.56) | |
| baseline RFA | 14.43 (± 3.71) | 13.90 (± 4.13) | 15.61 (± 3.33) | |
| Number of total follicles per randomization day | 18.55 (± 7.19) | 18.77 (± 5.06) | 18.88 (± 5.70) | |
| No. of follicles ≥ 16 mm day randomization | 9.30 (± 3.87) | 9.67 (± 3.10) | 9.70 (± 3.71) | |
| Maximum diameter (mm) | 21.75 (± 2.68) | 22.48 (± 2.12) | 21.80 (± 1.96) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Kruskal-Wallis |
| Comparison groups | 36 hours Group v 40 hours group v 30 hours Group |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Kruskal-wallis |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| lower limit | 0.49 |
| Variability estimate | Standard deviation |

Secondary: ESTRADIOL (pg/mL)

| | |
|-----------------|----------------------------------|
| End point title | ESTRADIOL (pg/mL) ^[2] |
|-----------------|----------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Time 0

Time 12h

Time puncion

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The research team decided that there was no significance in the 24h group, so no data was collected from it.

| End point values | 30 hours Group | 36 hours Group | 40 hours group | |
|--------------------------------------|--------------------|--------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 40 | 43 | 40 | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| E2 Time 0 | 1808.69 (± 778.60) | 1838.94 (± 804.63) | 2008.64 (± 937.73) | |
| E2 Time 12h | 1914.39 (± 919.37) | 2278.87 (± 860.12) | 2442.41 (± 1477.59) | |
| E2 Time P | 993.88 (± 530.63) | 875.20 (± 347.84) | 890.89 (± 440.11) | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Kruskal-Wallis |
| Comparison groups | 30 hours Group v 36 hours Group v 40 hours group |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 1-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 10 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| lower limit | 0.5 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unkown

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Non-severous |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | Non-severous | | |
|---|---------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Non-severous | | |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | | |
| Nervous system disorders | | | |
| cervical | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 24 November 2015 | Protocolo and patient information sheet and informed consent changes |
| 28 March 2017 | Protocol changes |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported