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 proceadures 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