



Clinical trial results:

Eight weeks of androgen priming by hCG before IVF/ICSI in women with low ovarian reserve.

Summary

EudraCT number	2020-002453-26
Trial protocol	DK
Global end of trial date	01 August 2021

Results information

Result version number	v1 (current)
This version publication date	21 December 2022
First version publication date	21 December 2022

Trial information

Trial identification

Sponsor protocol code	73908
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04643925
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Fertility Department, Rigshospitalet
Sponsor organisation address	Juliane Maries Vej 8, Copenhagen, Denmark, 2100
Public contact	Fertility Research , Rigshospitalet , fertilitet.rigshospitalet@regionh.dk
Scientific contact	Fertility Research , Rigshospitalet , fertilitet.rigshospitalet@regionh.dk

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 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2021
Global end of trial reached?	Yes
Global end of trial date	01 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to investigate in a paired design if eight weeks of hCG pre-treatment improves responsiveness to ovarian stimulation during IVF/ICSI in women with low ovarian reserve.

Protection of trial subjects:

Patients were asked about side effects at each trial visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 December 2020
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	Denmark: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 33 women were assessed for eligibility and 20 women were included. No patients were lost to follow up and data from all patients were included in the final analyses. Eligible women were recruited if they fulfilled the inclusion criteria and none of the exclusion criteria.

Pre-assignment

Screening details:

Patients in the fertility clinic were screened and offered to participate in the trial if they fulfilled the following inclusion criteria:

- age 18-40 years
- regular menstrual cycle between 23 and 35 days
- Anti-Müllerian hormone (AMH) < 6.29 pmol/L measured within six months before inclusion

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Whole trial
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Arm description:

All participants underwent the following:

1. A Control cycle: A standard IVF/ICSI cycle in the fixed GnRH-antagonist protocol using a daily dose of 300 IU rFSH initiated from cd 2-3 and the GnRH antagonist (Fyremadel 0.25 mg) from stimulation day 5-6 followed by blastocyst culture and a freeze-all strategy.

2. Followed by a ~60 day priming period with a daily dose of 260 IU hCG

3. Followed by a Study cycle: hCG priming by Ovitrelle 260 IE once daily for 8 weeks followed by a standard IVF/ICSI cycle in the fixed GnRH-antagonist protocol using a daily dose of 300 IU rFSH initiated from cd 2-3 and the GnRH antagonist (Fyremadel 0.25 mg) from stimulation day 5-6 followed by a single blastocyst transfer at day 5.

Arm type	Experimental
Investigational medicinal product name	Ovitrelle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 daily injection of 260 IU Ovitrelle

Number of subjects in period 1	Whole trial
Started	20
Completed	20

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	36.8		
standard deviation	± 3.2	-	
Gender categorical			
All participants were female.			
Units: Subjects			
Female	20	20	
Male	0	0	
Menstrual cycle length			
Units: day			
arithmetic mean	26.2		
standard deviation	± 1.9	-	

End points

End points reporting groups

Reporting group title	Whole trial
Reporting group description:	
All participants underwent the following:	
1. A Control cycle: A standard IVF/ICSI cycle in the fixed GnRH-antagonist protocol using a daily dose of 300 IU rFSH initiated from cd 2-3 and the GnRH antagonist (Fyremadel 0.25 mg) from stimulation day 5-6 followed by blastocyst culture and a freeze-all strategy.	
2. Followed by a ~60 day priming period with a daily dose of 260 IU hCG	
3. Followed by a Study cycle: hCG priming by Ovitrelle 260 IE once daily for 8 weeks followed by a standard IVF/ICSI cycle in the fixed GnRH-antagonist protocol using a daily dose of 300 IU rFSH initiated from cd 2-3 and the GnRH antagonist (Fyremadel 0.25 mg) from stimulation day 5-6 followed by a single blastocyst transfer at day 5.	
Subject analysis set title	Control cycle
Subject analysis set type	Full analysis
Subject analysis set description:	
All trial participants	
Subject analysis set title	Study cycle
Subject analysis set type	Full analysis
Subject analysis set description:	
All study participants	

Primary: FORT

End point title	FORT
End point description:	
FORT, defined as the number of pre-ovulatory follicles (>16 mm) on hCG trigger day divided by the number of antral follicles (2-10 mm) at baseline.	
End point type	Primary
End point timeframe:	
At the end of trial	

End point values	Control cycle	Study cycle		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20 ^[1]	20		
Units: Rate				
arithmetic mean (standard deviation)	0.4 (± 0.4)	0.4 (± 0.2)		

Notes:

[1] - All subjects in the trial

Statistical analyses

Statistical analysis title	Paired T-test
Statistical analysis description:	
Paired T-test for the difference in mean between FORT in the Control and Study cycle.	
Comparison groups	Control cycle v Study cycle

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Until trial completion date.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	All participants
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Reporting group description: -

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (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	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		

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: None of the study participants experienced any serious adverse events in the trial.

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