



Clinical trial results:

Optimizing serum progesterone level during luteal phase in hormone replacement therapy frozen embryo transfer (HRT-FET) cycle – interventional and observational trial

Summary

EudraCT number	2019-001539-29
Trial protocol	DK
Global end of trial date	20 December 2022

Results information

Result version number	v1
This version publication date	07 September 2023
First version publication date	07 September 2023

Trial information

Trial identification

Sponsor protocol code	alsbjerg1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	The Fertility Clinic, Skive Regional Hospital
Sponsor organisation address	Reservevej 25, Skive, Denmark, 7800
Public contact	The Fertility Clinic, Skive Regiona, The Fertility Clinic, Skive Regional Hospital, +45 78445760, birgit.alsbjerg@midt.rm.dk
Scientific contact	The Fertility Clinic, Skive Regiona, The Fertility Clinic, Skive Regional Hospital, +45 78445760, birgit.alsbjerg@midt.rm.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	20 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2022
Global end of trial reached?	Yes
Global end of trial date	20 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate the effect of adding progesterone rectally in hormone replacement treatment frozen embryo transfer (HRT-FET) cycles if the serum progesterone (P4) is <35nmol/l on embryo transfer day.

Protection of trial subjects:

The study was approved by the scientific Ethics Committee of the Central Denmark Region – Project number: M-2019-200-19

Written informed consent was obtained from all participants prior to inclusion

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 488
Worldwide total number of subjects	488
EEA total number of subjects	488

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)	488
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled in January 2020 and the last patient was enrolled in September 2022

Pre-assignment

Screening details:

A total of 607 patients were assessed for eligibility and 488 patients were subsequently recruited. No patient was lost to follow-up

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group <35 nmol/l

Arm description:

HRT treatment including 6 mg estradiol (Estrafem) and vaginally progesterone (Cyclogest) 400 mg twice a day. If serum P4 is <35 nmol/l at the day of embryo transfer the progesterone regime is changed to 400 mg vaginally Cyclogest and additional 400 mg Cyclogest administered rectally starting at the day of transfer.

Arm type	Experimental
Investigational medicinal product name	Cyclogest
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suppository
Routes of administration	Rectal use

Dosage and administration details:

(400mg/12hour starting that same day as embryo transfer. In pregnant patients, rectal administration continued until week 8 of gestation.

Arm title	Group >35 nmol/l
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Arm description:

HRT treatment including 6 mg estradiol (Estrafem) and vaginally progesterone (Cyclogest) 400 mg twice a day

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Group <35 nmol/l	Group >35 nmol/l
Started	114	374
Completed	114	374

Baseline characteristics

Reporting groups

Reporting group title	Group <35 nmol/l
Reporting group description: HRT treatment including 6 mg estradiol (Estrafem) and vaginally progesterone (Cyclogest) 400 mg twice a day. If serum P4 is <35 nmol/l at the day of embryo transfer the progesterone regime is changed to 400 mg vaginally Cyclogest and additional 400 mg Cyclogest administered rectally starting at the day of transfer.	
Reporting group title	Group >35 nmol/l
Reporting group description: HRT treatment including 6 mg estradiol (Estrafem) and vaginally progesterone (Cyclogest) 400 mg twice a day	

Reporting group values	Group <35 nmol/l	Group >35 nmol/l	Total
Number of subjects	114	374	488
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	114	374	488
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	30.9	30.9	
standard deviation	± 4.6	± 4.6	-
Gender categorical Units: Subjects			
Female	114	374	488
Male	0	0	0

Subject analysis sets

Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: The primary analysis was the full analysis of all included patients having an embryo transfer.	

Reporting group values	Full analysis		
Number of subjects	488		
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)	488		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	30.9		
standard deviation	± 4.6		
Gender categorical			
Units: Subjects			
Female	488		
Male	0		

End points

End points reporting groups

Reporting group title	Group <35 nmol/l
Reporting group description: HRT treatment including 6 mg estradiol (Estrofem) and vaginally progesterone (Cyclogest) 400 mg twice a day. If serum P4 is <35 nmol/l at the day of embryo transfer the progesterone regime is changed to 400 mg vaginally Cyclogest and additional 400 mg Cyclogest administered rectally starting at the day of transfer.	
Reporting group title	Group >35 nmol/l
Reporting group description: HRT treatment including 6 mg estradiol (Estrofem) and vaginally progesterone (Cyclogest) 400 mg twice a day	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: The primary analysis was the full analysis of all included patients having an embryo transfer.	

Primary: Ongoing pregnancy

End point title	Ongoing pregnancy
End point description:	
End point type	Primary
End point timeframe: 12 weeks	

End point values	Group <35 nmol/l	Group >35 nmol/l		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	374		
Units: percent				
number (not applicable)	46	45		

Statistical analyses

Statistical analysis title	X ² test
Comparison groups	Group <35 nmol/l v Group >35 nmol/l
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 1-sided

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

14 weeks

Adverse event reporting additional description:

No adverse events were reported during the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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Frequency threshold for reporting non-serious adverse events: 5 %

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: There was no non-serious adverse events. However, few side effects do to discharge.

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