



Clinical trial results:

Estradiol levels in early pregnancy after natural, estradiol + progesterone or gonadotrophin stimulated frozen embryo transfer (FET) cycle

Summary

EudraCT number	2020-001218-39
Trial protocol	DK
Global end of trial date	06 December 2024

Results information

Result version number	v1 (current)
This version publication date	19 November 2025
First version publication date	19 November 2025

Trial information

Trial identification

Sponsor protocol code	svenne0405
-----------------------	------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Borgmester Ib Juuls vej 9, Herlev, Denmark, 2730
Public contact	Fertility clinic Herlev University , Fertility clinic Herlev University Hospital, pernille.fog.svensen@regionh.dk
Scientific contact	Fertility clinic Herlev University , Fertility clinic Herlev University Hospital, +45 26208702, pernille.fog.svensen@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 May 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2024
Global end of trial reached?	Yes
Global end of trial date	06 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate plasma estradiol and progesterone levels in early pregnancy in women who have conceived after transfer of thawed blastocysts in an either natural or hormonstimulated cycle.

Protection of trial subjects:

Not relevant for this study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 April 2021
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: 305
Worldwide total number of subjects	305
EEA total number of subjects	305

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)	305
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from The Fertility Clinic at Herlev University Hospital from april 2021 untill December 2024

Pre-assignment

Screening details:

Patients could could participate in the study if they had frozen blastocysts.

Inclusion criteria:

Age > 18 years < 40 years

BMI < 35 kg/m²

Normal wet smear within the past three years

Thawed blastocysts (day 5) after either IVF or ICSI treatment

Exclusion criteria:

Age < 18 years

BMI > 35 kg/m²

Day 6 blastocysts

Oocyte donation

Pre-assignment period milestones

Number of subjects started	305
Number of subjects completed	305

Period 1

Period 1 title	Overall 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	modified natrural cycle for ovulatory women
------------------	---

Arm description:

FET in a natural cycle with ovulation trigger

Arm type	Active comparator
Investigational medicinal product name	ovitrelle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

250 mic grams

One injection

Arm title	programmed cycle for ovulatory women
------------------	--------------------------------------

Arm description:

Estradiol and progesterone administartion

Arm type	Active comparator
----------	-------------------

Investigational medicinal product name	estradiol
Investigational medicinal product code	
Other name	østradiol
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
6-8 mg daily	
Investigational medicinal product name	cyclogest
Investigational medicinal product code	progesterone
Other name	
Pharmaceutical forms	Vaginal tablet
Routes of administration	Vaginal use, Rectal use
Dosage and administration details:	
400 mg three times daily	
Arm title	gondotrophin stimulated cycle for anovulatory women
Arm description:	
FET using gonadotrophin stimulation and ovulation trigger	
Arm type	Active comparator
Investigational medicinal product name	bemfola
Investigational medicinal product code	recombinant follitropin alpha
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details:	
50 - 75 IU starting dose increasing until follicular growth	
Investigational medicinal product name	ovitrelle
Investigational medicinal product code	HCG
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details:	
250 mic grams once	
Arm title	programmed cycle for anovulatory women
Arm description:	
Estradiol and progesterone administration	
Arm type	Active comparator
Investigational medicinal product name	estradiol
Investigational medicinal product code	
Other name	østradiol
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
6-8 mg daily	
Investigational medicinal product name	cyclogest
Investigational medicinal product code	
Other name	progesterone
Pharmaceutical forms	Vaginal tablet
Routes of administration	Vaginal use, Rectal use
Dosage and administration details:	
400 mg three times daily	

Number of subjects in period 1	modified natural cycle for ovulatory women	programmed cycle for ovulatory women	gonadotrophin stimulated cycle for anovulatory women
Started	116	116	36
Completed	102	107	31
Not completed	14	9	5
Protocol deviation	14	9	5

Number of subjects in period 1	programmed cycle for anovulatory women
Started	37
Completed	33
Not completed	4
Protocol deviation	4

Baseline characteristics

End points

End points reporting groups

Reporting group title	modified natural cycle for ovulatory women
Reporting group description: FET in a natural cycle with ovulation trigger	
Reporting group title	programmed cycle for ovulatory women
Reporting group description: Estradiol and progesterone administration	
Reporting group title	gonadotrophin stimulated cycle for anovulatory women
Reporting group description: FET using gonadotrophin stimulation and ovulation trigger	
Reporting group title	programmed cycle for anovulatory women
Reporting group description: Estradiol and progesterone administration	

Primary: Estradiol levels

End point title	Estradiol levels
End point description:	
End point type	Primary
End point timeframe: 20/4-2021-6/12-2024	

End point values	modified natural cycle for ovulatory women	programmed cycle for ovulatory women	gonadotrophin stimulated cycle for anovulatory women	programmed cycle for anovulatory women
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102	107	31	33
Units: nmol/l				
number (not applicable)	102	107	31	33

Statistical analyses

Statistical analysis title	Welch's two-sample t-test or Mann-Whitney
Statistical analysis description: Comparisons between treatment groups of reproductive outcomes and obstetric data were performed by Welch's two-sample t-test or Mann-Whitney test for continuous data and by Fisher's exact test for categorical data. We used a linear mixed model (LMM) including GA (categorical as visits) as a fixed effect to analyze changes in estradiol and progesterone over time. T	
Comparison groups	modified natural cycle for ovulatory women v programmed cycle for ovulatory women v gonadotrophin stimulated cycle for anovulatory women v programmed cycle for anovulatory

	women
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
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

Timeframe for reporting adverse events:

Treatment start until one week after administration of the last dose of study medication

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

Dictionary used

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

Dictionary version	1
--------------------	---

Reporting groups

Reporting group title	Modified natural cycle
-----------------------	------------------------

Reporting group description: -

Serious adverse events	Modified natural cycle		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 102 (0.98%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy	Additional description: Treated by standard protocol		
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1.5 %

Non-serious adverse events	Modified natural cycle		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 102 (29.41%)		
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 102 (29.41%)		
occurrences (all)	30		

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