A phase III, randomized, double-blind, active-controlled, non-inferiority clinical trial to investigate the efficacy and safety of a single injection of Org 36286 (corifollitropin alfa) to induce multifollicular development for controlled ovarian stimulation using daily recombinant FSH as a reference

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38819: To investigate the efficacy and safety of a single injection of Org 36286 to induce multifollicular development for COS using daily recFSH as a reference.38821: To evaluate whether Org 36286 treatment for the induction of multifollicular...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON29984

Source
ToetsingOnline

Brief title
Nvt

Condition

- Other condition
- Endocrine disorders of gonadal function

Synonym
Infertility

Health condition

Infertiliteit

Research involving
Human

Sponsors and support

Primary sponsor: Organon Nederland bv
Source(s) of monetary or material Support: vanuit Organon

Intervention

Keyword: 38819:, 38821:, 38831:, follow-up, frozen-thawed embryo transfer cycle., IVF/ICSI., Org 36286, phase III, pregnancy., rec FSH

Outcome measures

Primary outcome

38819:

pregnancy

Note:

38821 (evaluation): pregnancy, mode of delivery, neonatal outcome.

38831 (evaluation): number and quality of the embryos transferred after thawing

and the outcome of the FTET cycle.

Secondary outcome

38819:

number of oocytes retrieved

safety: ((S)AEs, occurence of moderate/severe OHSS and antibody formation)

Study description

Background summary

Induction of multifollicular development in women undergoing conventional in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) commonly rely on multiple injections of FSH preparations. Development of new treatment regimens requiring fewer injections is considered an advancement. To this end Org 36286 (corifollitropin alfa) was developed. Given the pharmacokinetic profile, a single injection of Org 36286 results in sustained follicular stimulation and may replace the first 7 injections of any FSH preparation in controlled ovarian stimulation (COS) for assisted reproductive technology (ART).

The available pre-clinical and clinical data on Org 36286 show that the compound has a prolonged half-life and a higher in vivo bioactivity as compared to that of recombinant human FSH (follitropin beta). Efficacy of Org 36286 has been investigated. The results of the dose-finding trial indicated a significant dose-response relationship with respect to the number of cumulus-oocyte-complexes retrieved.
To date, more than 400 subjects have been treated with Org 36286 in phase I and II trials. It is concluded that in these trials, Org 36286 was safe and well-tolerated.

Study objective

38819:
To investigate the efficacy and safety of a single injection of Org 36286 to induce multifollicular development for COS using daily recFSH as a reference.
38821:
To evaluate whether Org 36286 treatment for the induction of multifollicular growth in women undergoing controlled ovarian stimulation (COS) is safe for pregnant subjects and their offspring.
38831:
To collect the outcome of FTET cycles performed after embryos are cryopreserved in trial 38819 in order to estimate the cumulative pregnancy rate for each treatment group.

Study design

38819:
This is a randomized, double blind, active controlled, non-inferiority clinical trial

38821:
pregnancy and neonatal follow-up protocol
38831:
FTET cycle outcome follow-up protocol

Intervention

Investigational group:
-Org 36286: single SC injection of 150 µg (0.5 mL): day 1*
-placebo-recFSH (equivalent of 200 IU fixed dose) (daily): day 1 u/i day 7
-recFSH (max 200 IU)(daily from day 8)
-hCG (5.000 or 10.000 IU/USP Units): as soon as 3 follicles > or = 17mm

Reference group:
-placebo Org 36286; single SC injection of 150 µg (0.5 mL): day 1*
-recFSH (SC injection 200 IU fixed dose): day 1 u/i day 7
-recFSH (max 200 IU)(daily from day 8)
-hCG(5.000 or 10.000 IU/USP Units): as soon as 3 follicles > or = 17mm

Both groups:
-Ganirelix (0.25 mg) (SC injection): day 5 u/i day hCG
-micronized progesterone (at least 600 mg/day, vaginally or at least 50 mg/day, intramuscularly (IM)): day OPU till 6 weeks or menses or up to negative pregnancy test performed at least 14 days after embryo transfer.

* Stimulation day 1 is day 2 or 3 of menstrual cycle

Study burden and risks

Risks:
Headache, nausea and fatique have been reported during treatment with Org 36286, FSH preparations and GnRH analogues (other medication used during infertility treatment). General risks associated with ovarian stimulation are e.g. pelvic pain, overstimulation, multiple pregnancy, ectopic pregnancy, etc.

Benefits:
It is anticipated that Org 36286 may be beneficial in further reducing the number of FSH injections for patients undergoing ovarian stimulation for IVF or ICSI. Patients will be thoroughly monitored throughout the study.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

38819:
-Females of couples with an indication for COS and IVF or ICSI;
- >18 and <36 years of age at the time of signing informed consent;
-Body weight > 60 and < 90 kg and BMI > 18 and < 32 kg/m2;
-Normal menstrual cycle length: 24-35 days;
-Availability of ejaculatory sperm (use of donated and/or cryopreserved sperm is allowed)
38821:
-Subjects who received at least one dose of either Org 36286 or Puregon/Follistim in trial 38819
-Ongoing pregnancy confirmed by ultrasound at least 10 weeks after embryo transfer in trial 38819
38831:
-Subjects from whom embryos have been cryopreserved in trial 38819 of which at least one embryo is thawed for use in a subsequent FTET cycle.

Exclusion criteria

38819:
-More than 20 basal antral follicles <11 mm (both ovaries combined) as measured on USS in the early follicular phase (menstrual cycle day 2-5);
-Less than 2 ovaries or any other ovarian abnormality (including endometrioma > 10 mm; visible on USS);
-Presence of unilateral or bilateral hydrosalphinx (visible on USS);
-Presence of any clinically relevant pathology affecting the uterine cavity or fibroids >5 cm;
-More than three unsuccessful IVF cycles since the last established ongoing pregnancy (if applicable);
-History of non- or low ovarian response to FSH/hMG treatment;
-History of recurrent miscarriage (3 or more, even when unexplained);
-FSH > 12 IU/L or LH > 12 IU/L as measured by the local laboratory (sample taken during the early follicular phase: menstrual cycle day 2-5);
-Previous use of Org 36286;
-Use of hormonal preparations within 1 month prior to randomization;

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2006
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Org 36286
Generic name:	corifollitropin alfa
Product type:	Medicine
Brand name:	RecFSH (Puregon)
Generic name:	follitropin beta
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-05-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-09-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-01-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-02-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-07-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-08-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	08-01-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-09-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-10-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR38819:2004-004-NL
CCMO	NL11790.041.06
Other	Zie www.organon-trials.com