The efficacy of GnRH antagonists in cycles with mild ovarian hyperstimulation with recFSH in an intrauterine insemination program. A randomised placebo-controlled double-blinded investigator initiated study.

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We hypothesize that the use of a GnRH-antagonist in cycles with Mild Ovarian Hyperstimulation (MOH) combined with Intrauterine insemination (IUI) programs significantly improves live birth rates compared with MOH and a placebo.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22749

Bron
Nationaal Trial Register

Verkorte titel
IUI study IMP 26162

Aandoening

Eligible for consideration are couples who are primarily undesirably non-pregnant and for whom an IUI procedure is suggested as a viable treatment option.
A routine fertility check-up as defined, for instance, in the guidelines of the Dutch Society of Obstetrics and Gynaecology will be performed in this study. This defines the concepts of subfertility, previous history, physical examination (in this study including recording of the height and weight), laboratory tests and fertility work-up.

Ondersteuning

Primaire sponsor: none

Serono Benelux B.V. will provide all centres with the necessary drugs
Overige ondersteuning: Stichting Onderzoek en Onderwijs Voortplantingsgeneeskunde Zwolle S.O.O.V.Z.

Serono Benelux B.V.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Live birth rate per couple.

Toelichting onderzoek

Achtergrond van het onderzoek

Accurate timing of insemination is one of the most important variables that affect the result of intrauterine insemination (IUI).
The onset of the preovulatory luteinizing hormone (LH) surge is one of the best indicators of the initiation of ovulation.
The LH rise can be detected in blood. In cycles with ovarian stimulation spontaneous LH surges occur in 25% of the cases, hardly resulting in any pregnancy and are therefore useless.

Luteinizing hormone surges can be prevented by administering a GnRH-antagonist. When used from a mean diameter of 14 mm of the dominant follicle(s) onwards, it has to be applied for a few days.
Preventing LH surges with administering an effective drug might be cost-effective.
It seems therefore logical to perform a large multicentre randomised controlled trial to investigate the efficacy of applying a GnRH-antagonist in MOH/IUI programs.
The results of a multi-centre trial were presented at the ESHRE 2004, showing effective suppression of LH surges by the antagonist, but no significant differences in pregnancy rates.
The authors stated that larger multi-centre double-blinded placebo-controlled trials are mandatory.

The aim of the study is to examine the efficacy of GnRH-antagonists in cycles with ovarian

stimulation with recombinant Follicle Stimulating Hormone (FSH) combined with IUI.

This will be done in a prospectively randomised placebo controlled trial in couples with unexplained and mild male subfertility for at least 2 years.

Use will be made of recombinant FSH (Gonal-F, Serono Benelux). 75 IU Gonal-F will be administered daily subcutaneously. Gonal-F stimulation will start on cycle day 2 to 4.

From a follicle size of at least 14 mm onwards Cetrorelix (Cetrotide, Serono Benelux) 0.25 mg will be administered subcutaneously or an equal volume equivalent of placebo.

Rec-hCG (250 Î¼g Ovitrelle, Serono Benelux) will be administered on the day that the size of the largest follicle is at least 18 mm. Once-only insemination will take place 38-40 hours after administration of Ovitrelle.

Live birth rates will be treated as primary end points. Pregnancy rates per couple, the occurrence of spontaneous LH surges and premature luteinization, multiple pregnancy rates, miscarriage rates and rates of ectopic pregnancies, total costs and cost-effectiveness will be secondary end-points.

Because this study will be the same as the standard treatment the patients will not be exposed to additional risks. Except the injection of cetrorelix for a couple of days and the withdrawal of blood on the day of hCG no extra events will take place compared to the standard treatment.

Doel van het onderzoek

We hypothesize that the use of a GnRH-antagonist in cycles with Mild Ovarian Hyperstimulation (MOH) combined with Intrauterine insemination (IUI) programs significantly improves live birth rates compared with MOH and a placebo.

Onderzoeksproduct en/of interventie

The research group of patients will consist of two arms:
one group will receive ovarian stimulation with recFSH combined with placebo (the recFSH group)
and one group will receive recFSH combined with a GnRH-antagonist (the recFSH-anta group).
Both ovarian stimulation protocols will be followed by intrauterine insemination.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Primary and secondary subfertile patients between 18 and 35 years of age with a diagnosis of unexplained or mild male infertility (see above) will be included.

Definition of unexplained subfertility:
normozoospermia using the guidelines of the WHO;
patent Fallopian tubes (both ovaries should be in situ);
cycles varying between 24 and 35 days with an indication of ovulation;
no abnormalities at laparoscopy and/or hysterosalpingography.

Information from the post-coital test when performed will only be used for a prognostic model and not as an exclusion criterion.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Age of the woman < 18 or > 35 years;

2. Duration of subfertility below 2 years;

3. Manifest pathology of the Fallopiantubes;

4. Severe forms of endometriosis (when laparoscopy has been performed: > AFS II);

5. An average total number of motile spermatozoa during semen analysis (performed twice in case of abnormal findings) below 10 million;

6. Cycle disturbances (where otherwise ovulation induction would be used);

7. Previous IUI or IVF/ICSI treatment;

8. If an initial ultrasound shows an image of a cyst that is larger than 25 mm treatment will be postponed for 1 month. Persistence of a cyst is a reason for exclusion;

9. Contraindications for recFSH (Gonal-F), rec-hCG (Ovitrelle) and Cetrotide.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland
Status: Werving nog niet gestart

(Verwachte) startdatum:	15-11-2005
Aantal proefpersonen:	520
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	06-11-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL456
NTR-old	NTR497
Ander register	: N/A
ISRCTN	ISRCTN15295216

Resultaten

Samenvatting resultaten
N/A