# TOPFIT: Triptorelin Oral contraceptive Pill Flare-up in IVF/ICSI Treatment trial The effect of a short, flare-up gonadotrophin-releasing hormone agonist versus antagonist treatment protocol in patients pre-treated with oral contraceptive pill on premature luteinizing hormone surges

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Sexual function and fertility disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON34327

**Source**
ToetsingOnline

**Brief title**
TOPFIT-trial

### Condition

- Sexual function and fertility disorders

**Synonym**
infertility, IVF/ICSI treatment

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** Stichting Wetenschappelijk Onderzoek Gynaecologie (SWOG)

## Intervention

**Keyword:** gonadorelin (GnRH) agonist, gonadorelin (GnRH) antagonist, IVF/ICSI, subfertility

## Outcome measures

### Primary outcome

The primary endpoint is the incidence of premature LH surges, defined as a serum LH value > 10 IU/l, with or without a rise in progesterone, defined as a value > 1 ng/ml (> 3.18 nmol/l).

### Secondary outcome

Secondary endpoints include incidence of premature urine LH surges, follicular development, number of oocytes and (top-quality) embryo*s, embryo metabolomics, endometrial thickness, hormone levels (LH, FSH, oestradiol, progesterone), (signs of) ovarian hyperstimulation syndrome (OHSS), cancellation rate, fertilisation rate, implantation rate, ongoing pregnancy rate and live birth rate. In addition, (hypo-oestrogenic) adverse events and total dose and duration of GnRH analogue and gonadotrophin treatment will be assessed.

# Study description

## Background summary

In contrast to the long gonadotrophin releasing hormone (GnRH)-agonist protocol, the GnRH-antagonist protocol is associated with the occurrence of premature luteinizing hormone (LH) surges. In clinical practice, pre-treatment with oral contraceptive (OC) pill is given to enhance follicle synchronisation and, as a consequence, to minimize premature ovulation, although the latter is still reported to occur. A so called short or flare-up GnRH-agonist protocol is also used in clinical practice as patient-friendly alternative to the long protocol. Little is known on the incidence of premature LH surges under this protocol; and whether these can be pre-empted by OC pill pre-treatment. To date, no comparison has been made between the short GnRH-agonist protocol versus the GnRH-antagonist protocol, both combined with OC pill pre-treatment with respect to their efficacy in preventing premature LH surges.

## Study objective

The aim of the study is to show non-inferiority of a short, flare-up GnRH-agonist protocol to the GnRH-antagonist protocol, both with OC pill pre-treatment, in women undergoing in vitro fertilisation (IVF) or intracellular sperm injection (ICSI) treatment with gonadotrophins. Primary endpoint will be the incidence of premature serum LH surges.

## Study design

The study has an open, prospective, multi-centre, parallel two-arm randomised controlled design.

## Intervention

1. Flare-up GnRH-agonist protocol with OC pill pre-treatment. OC pill is given during 21±3 days of the preceding cycle. On day two of the menses after withdrawal of the OC pill of the following cycle, triptorelin is started, accompanied at day three by HP-hMG in a fixed dose of 150 IU. Both are given until criteria for hCG administration are met.

2. GnRH-antagonist protocol with OC pill pre-treatment. OC pill is given during 21±3 days of the preceding cycle. On day three of the menses of the following cycle, HP-hMG (fixed dose of 150 IU) is started and accompanied by cetrorelix at day six of gonadotrophin administration, both given until criteria for hCG administration are met.

## Study burden and risks

This study is ethically justified, since the study has a non-inferiority design relative to currently used treatment. During this study every participant has

an equal chance to profit from the possible benefits. The measurements during this study will be combined as much as possible with the routine investigations. All medication used in this study is registered for the given indication and used in clinical practice for years. During the entire study period possible side effects and severe adverse events will be monitored and evaluated.
Combining the short, GnRH-agonist and *antagonist protocol with OC pill pre-treatment probably leads to better synchronization of follicular development and possibly better effectiveness. No untoward effects on the treatment results (chance to become pregnant) are envisaged. Possible benefits are improving patient comfort by minimizing the number of GnRH-analogue injections.

## Contacts

**Public**
Vrije Universiteit Medisch Centrum

Amstelveenseweg 601
1081 JC Amsterdam
NL
**Scientific**
Vrije Universiteit Medisch Centrum

Amstelveenseweg 601
1081 JC Amsterdam
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

- IVF or ICSI treatment (first, second or third cycle)
- Signed informed consent

### Exclusion criteria

- Women aged over 39 years
- Women with a single ovary
- Known poor responders, defined as women with a follicle count of < 4 follicles > 14 mm in a previous IVF/ICSI treatment cycle
- History or evidence of polycystic ovary syndrome (PCOS) or incipient ovarian failure (IOF)
- Severe endometriosis, stage III/IV, needing Surrey stimulation protocol
- Women with known contraindications for oral OCs

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-01-2011 |
| Enrollment: | 200 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Cetrotide |

| | |
|---|---|
| Generic name: | cetrorelix |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Decapeptyl |
| Generic name: | triptorelin |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 21-09-2010 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-09-2010 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

## 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 | EUCTR2010-022171-56-NL |
| CCMO | NL32470.029.10 |