

# An additional rescue dose of GnRH antagonist administered the day before hCG trigger is effective to prevent ovarian hyperstimulation syndrome (OHSS) in IVF/ICSI antagonist cycles at risk for OHSS without affecting the reproductive outcomes

<b>Submission date</b> 13/07/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 13/08/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 19/10/2017	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Gonadotrophin releasing hormone (GnRH) antagonists are compounds that are similar to the natural hormone but have an opposite effect. Treatment with GnRH antagonists lowers but does not eliminate the risk of ovarian hyperstimulation syndrome (OHSS) in hyper-responding patients who are undergoing in vitro fertilisation (IVF/ICSI cycles). A double daily GnRH antagonist dose given for 1-3 days before a process called human chorionic gonadotrophin (hCG) triggering seems to eliminate the risk of OHSS in oocyte donation cycles. In addition, GnRH agonist triggering for final oocyte maturation reduces pregnancy rates. The aim of this study was to find out the prevalence of early and late OHSS as well as the pregnancy rate in patients at risk for OHSS, stimulated with the antagonist who received a double dose of the antagonist regiment (Ganirelix) for a single day, with a reducing daily dose of follicle stimulating hormone (FSH). These patients were compared with a control group of patients at a high risk for OHSS who did not receive the double dose of the antagonist regiment, with a reducing dose of FSH.

### Who can participate?

The study included patients at high risk for OHSS who underwent ovarian stimulation for IVF using the 6th day fixed GnRH antagonist method. Patients were aged above 18 years but younger than 40 years, with polycystic ovaries.

### What does the study involve?

Participants were randomly allocated to one of two groups: Intervention Group A and Control Group B. Group A received a double dose of GnRH antagonist the day before hCG while control group B did not. In both groups FSH dosage was reduced to 100IU on the day of the allocation.

What are the possible benefits and risks of participating?

Patients can benefit by avoiding cancellation of their IVF cycle and proceed to fresh embryo transfer with safety. A rescue double GnRH antagonist dose the day before hCG trigger may effectively be a safe alternative preventive strategy for early and late OHSS without affecting the pregnancy outcomes. The main risks for the patients is that since the intervention proposed is new with lack of robust references regarding the safety of approach, OHSS can still occur and cycle cancellation might still be suggested as a preventive measure after all.

Where is the study run from?

The study is run from a private fertility centre IAKENTRO in Thessaloniki, Greece

When is study starting and how long is it expected to run for?

November 2009 to February 2013

Who is funding the study?

IAKENTRO fertility centre (Greece)

Who is the main contact?

Professor Yannis Prapas, yannis@iakentro.gr

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## Contact information

### Type(s)

Scientific

### Contact name

Prof Yannis Prapas

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## Additional identifiers

### Protocol serial number

N/A

## Study information

### Scientific Title

An additional rescue dose of GnRH antagonist administered the day before hCG trigger is effective to prevent OHSS in IVF/ICSI antagonist cycles at risk for OHSS without affecting the reproductive outcomes: a prospective randomized controlled trial

### Study objectives

In GnRH antagonist IVF/ICSI cycles at risk for ovarian hyperstimulation syndrome (OHSS), is a double antagonist dose (0,25mg/12h) administered the day before hCG trigger, effective to prevent OHSS without affecting the reproductive outcomes?

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Institutional Review Board; ref. 11/2009

### **Study design**

Prospective randomized controlled trial

### **Primary study design**

Interventional

### **Study type(s)**

Prevention

### **Health condition(s) or problem(s) studied**

Ovarian hyperstimulation syndrome (OHSS), ovarian stimulation, GnRH antagonist, IVF

### **Interventions**

Patients were randomised to:

1. Intervention group A (down-regulate FSH daily dose to 100 iu, up until hCG trigger and receive double GnRH antagonist dose the day before hCG trigger)
2. Control group B (down-regulate FSH daily dose to 100 iu, up to the hCG trigger)

Patients were considered at actual risk of developing moderate to severe OHSS when they had a high or rapidly rising serum estradiol ( $\geq 3500$  pg/ml before oocyte maturation and projected to be  $>4500$  pg/ml the day of hCG administration) and 18 or more follicles  $\geq 11$  mm but without any mature follicle  $>16$  mm appearing at that time. A standard fixed 6th day antagonist protocol (Orgalutran 0.25 mg, Organon) with 225 IU/day recombinant FSH (rFSH, Puregon Organon) starting on day 2 of the cycle was used for the ovarian stimulation. In the 5th and 7th day of stimulation the rFSH daily dose, if needed, was adjusted according to ovarian response, accounting ultrasound control of growing follicles and oestradiol levels (blood sample). The criteria for the allocation of patients to the study groups were met from the 7th day of stimulation and onwards. Final oocyte maturation was achieved by administration of 10.000 IU of hCG (Pregnyl, NV Organon, the Netherlands) as soon as three or more follicles of  $\geq 17$ mm were present on ultrasound control. Transvaginal oocyte aspiration was performed 36 hours after hCG administration by ultrasound-guided follicle puncture. All women were examined clinically and by ultrasound three and five days after oocyte retrieval or earlier if any discomfort appeared, for signs of moderate or severe OHSS using grading criteria (Golan et al., 1989; Grossman et al., 2010). If these symptoms of OHSS were present, the embryo transfer was cancelled, all embryos were cryo-preserved at the stage of blastocyst. Patients in both groups, without signs of OHSS had at least one embryo transferred on day 5 after OPU (blastocyst stage). A pregnancy test was performed 15 days after embryo transfer. The concurrency of a positive  $\beta$ -hCG test and a fetal heart beat (seen by ultrasound at 7 weeks of gestation) was defined as a clinical pregnancy, otherwise it was considered a biochemical pregnancy.

**Intervention Type**

Other

**Phase**

Not Applicable

**Primary outcome(s)**

1. Early and late OHSS rates
2. Clinical pregnancy rate

**Key secondary outcome(s)**

1. Oestradiol (E2)
2. Luteizing hormone (LH)
3. Progesterone (PR) levels

**Completion date**

28/02/2013

**Eligibility****Key inclusion criteria**

1. Patients age 18-40 years, at high risk for OHSS who underwent ovarian stimulation for in vitro fertilization (IVF) using the 6th day fixed GnRH antagonist protocol. Patients were considered at actual risk of developing moderate to severe OHSS when they had a high or rapidly rising serum estradiol ( $\geq 3500$  pg/ml before oocyte maturation and projected to be  $>4500$  pg/ml the day of hCG administration) and 18 or more follicles  $\geq 11$  mm but without any mature follicle  $>16$  mm appearing at that time.
2. With polycystic ovaries (The Rotterdam ESHRE/ASRM-sponsored PCOS consensus Workshop Group, 2004)
3. At high risk for OHSS
4. Not willing to cancel their IVF cycle

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

40 years

**Sex**

Female

**Key exclusion criteria**

Polycystic ovarian syndrome (PCOS) patients

**Date of first enrolment**

01/11/2009

**Date of final enrolment**

28/02/2013

**Locations****Countries of recruitment**

Greece

**Study participating centre**

IAKENTRO

Thessaloniki

Greece

54250

**Sponsor information****Organisation**

IAKENTRO (Greece)

**ROR**

<https://ror.org/05mnrce88>

**Funder(s)****Funder type**

Hospital/treatment centre

**Funder Name**

IAKENTRO fertility centre (Greece)

**Results and Publications**

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/11/2017		Yes	No