

# Purified urinary follicle stimulating hormone (FSH) and recombinant FSH follitropin-alpha for polycystic ovarian syndrome (PCOS) patients undergoing intra-cytoplasmic sperm injection (ICSI)

**Submission date**

21/06/2009

**Recruitment status**

No longer recruiting

☐ Prospectively registered

☐ Protocol

**Registration date**

21/07/2009

**Overall study status**

Completed

☐ Statistical analysis plan

☐ Results

**Last Edited**

21/07/2009

**Condition category**

Nutritional, Metabolic, Endocrine

☐ Individual participant data

☐ Record updated in last year

**Plain English summary of protocol**

Not provided at time of registration

## Contact information

**Type(s)**

Scientific

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

## Secondary identifying numbers

N/A

# Study information

### Scientific Title

Prospective randomised study comparing purified urinary follicle stimulating hormone (FSH) (Fostimon®) and recombinant FSH Follitropin-alpha (Gonal-f®) for polycystic ovarian syndrome (PCOS) patients undergoing intra-cytoplasmic sperm injection (ICSI)

### Study objectives

Follicle-stimulating hormone is a heterodimer composed of an alpha-subunit and beta-subunit with glycosylation sites located on each of the subunits. The oligosaccharide attached to the FSH molecule terminates in a negatively charged residue, thereby forming a variety of isoforms that differ in their isoelectric points. The acidic isoforms were found to have a reduced bioactivity, as assessed by its potency for stimulating cyclic adenosine monophosphate production and by a longer half-life time in the circulation compared with the less acidic isoforms.

It has been suggested that different glycoforms may encode for different functions or have enhanced activity for a particular function. It was hypothesised that not only the quantity but also the quality of FSH, in terms of isoforms, plays an important role in the early follicular phase.

In a small pilot study performed to determine the predictive value of FSH isoforms for the outcome of IVF treatment, no statistical differences could be found in the isoform-composition between poor and good responders. They concluded that it is not likely that FSH isoforms predict treatment outcome after IVF.

To evaluate whether the FSH isoform composition affected the efficacy of a product, a meta-analysis was performed that compared a preparation expressing an acidic isoform profile (urinary-derived Metrodin-HP) with a preparation rich in less acidic isoforms (recombinant derived Gonal-f®). A total of five randomised clinical trials that specifically compared these two preparations was identified and included in the analysis. All parameters relating to the direct effect of FSH on the follicle differed significantly in favour of the product rich in less acidic isoforms, while data on pregnancy outcome did not reach significance. It is suggested that the FSH isoform profile of commercial gonadotrophin preparations is of clinical importance and should be taken into account when evaluating efficacy. However, FSH isoform composition has received little or no attention and is considered of negligible clinical effect.

The polycystic ovarian disease model would be ideal to test the possible different effects of gonadotrophins with different isoforms on the quality of oocytes.

PCOS patients were excluded from all phase III studies comparing urinary FSH with recombinant FSH. PCOS patients are also difficult patients to treat in in-vitro fertilisation (IVF) because of the difficulty to achieve optimum stimulation and the high risk of ovarian hyperstimulation syndrome (OHSS). A large percentage of PCOS patients has a high body mass index and this adds more difficulty to stimulation protocols. It was reported that the quality of oocytes in PCOS patients is inferior to the non PCOS patients, however, the pregnancy rate is the same because of the large number of oocytes retrieved in PCOS patients.

It would be interesting to find out if using purified FSH (Fostimon®) would have a different effect on oocyte quality as compared to recombinant FSH as the two products have different

isoform structure. ICSI will be used for all patients to verify the number and percentage of MII oocytes.

### **Ethics approval required**

Old ethics approval format

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

Internal Ethics Committee of the Egyptian IVF Center approved on the 29th September 2008.

### **Study design**

Prospective randomised controlled study

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

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

Treatment

### **Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

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

Polycystic ovarian syndrome

### **Interventions**

After the gonadotropin releasing hormone analogue (GnRHa) protocol a start dose of 2 - 3 ampoules of FSH (purified urinary FSH [Fostimon®] or recombinant FSH Follitropin-alpha [Gonal-f®]), depending on age and weight of patient, was provided. From day 6 of stimulation adjustments were performed. The frequency of oestradiol (E2) depended on the number of follicles. Ovulation was triggered when the follicle reached 18 mm (according to routine protocol).

ICSI and embryo transfer were performed on all patients as a routine procedure.

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

Purified urinary follicle stimulating hormone (FSH) (Fostimon®) or recombinant FSH Follitropin-alpha (Gonal-f®)

**Primary outcome measure**

Measured on day of oocyte retrieval:

1. Number and percentage of mature oocytes
2. Quality of oocytes

**Secondary outcome measures**

Measured from day of embryo transfer up to 7 weeks:

1. Number of grade I embryos
2. Implantation rate
3. OHSS rate
4. Number of ampoules of FSH

**Overall study start date**

01/11/2008

**Completion date**

31/05/2009

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

1. Aged between 18 and 37 years, female
2. Body mass index (BMI) 19 - 32 kg/m<sup>2</sup>
3. FSH below 10
4. World Health Organization (WHO) group II women with PCOS (Rotterdam criteria)
5. Indication for ICSI as male factor, tubal factor, long standing infertility not responding to other lines of treatment in PCOS patients

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

37 Years

**Sex**

Female

**Target number of participants**

84 patients

**Key exclusion criteria**

1. Previous failed IVF/ICSI
2. General medical disorders, diabetes, hypertension, thyroid disturbance, or hyperprolactinemia
3. Intrauterine lesions or fibroids
4. Non-obstructive azoospermia

**Date of first enrolment**

01/11/2008

**Date of final enrolment**

31/05/2009

## Locations

**Countries of recruitment**

Egypt

**Study participating centre**

10 Gesiret El Arab St.

Cairo

Egypt

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## Sponsor information

**Organisation**

Institut Biochimique SA (IBSA) (Switzerland)

**Sponsor details**

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PO Box 266

Pambio-Noranco

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6915

**Sponsor type**

Industry

**Website**

<http://www.ibsa-international.com>

**ROR**

<https://ror.org/051tj3a26>

# Funder(s)

## Funder type

Industry

## Funder Name

Institut Biochimique SA (IBSA) (Switzerland)

# Results and Publications

## Publication and dissemination plan

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration