ISRCTN36808716 https://doi.org/10.1186/ISRCTN36808716

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	Recruitment status	[ ] Prospectively registered
21/06/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/07/2009	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
21/07/2009	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Mohamed Aboulghar

Contact details
10 Gesiret El Arab St.
Mohandessin
Cairo
Egypt
12411

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 clicnical 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^2
3. FSH below 10
4. World Health Organization (WHO) group II women with PCOS (Roterdam 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
12411

Sponsor information

Organisation
Institut Biochimique SA (IBSA) (Switzerland)

Sponsor details
Via del Piano
PO Box 266
Pambio-Noranco
Lugano
Switzerland
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