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Trial evaluating the influence of morphology and developmental rate on euploid blastocysts ongoing implantation rate

Submission date
10/12/2013

Recruitment status
No longer recruiting

Registration date
20/01/2014

Overall study status
Completed

Last Edited
20/10/2017

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Preimplantation Genetic Screening (PGS) is a technique that is used to identify euploid embryos (embryos with a balanced set of chromosomes) among those produced by a couple during IVF. PGS is mainly carried out at day 5 or 6 after fertilization. Performing PGS at this stage requires the embryos to be frozen in order to perform a single embryo transfer. Those embryos found to be euploid are thawed and transferred to the uterus. Euploid embryos have a higher rate of implantation in the uterus. However, clear evidence is still missing about the usefulness of factors such as morphology (shape) and developmental rate in predicting implantation potential. The aim of this study is to find out whether these factors could be used to predict the implantation potential of euploid embryos after frozen single embryo transfer.

Who can participate?
Patients who are undergoing PGS at the G.EN.E.R.A. Centre for Reproductive Medicine (Italy)

What does the study involve?
The embryos are grouped into four classes according to morphology (excellent, good, average and poor) and into two classes according to developmental rate (slower-growing and faster-growing). The embryo to be transferred is randomly selected independently from morphological and developmental factors, and the implantation rates in the different classes are compared.

What are the possible benefits and risks of participating?
The study will provide evidence of the influence of morphology and developmental rate on the developmental potential of embryos.

Where is the study run from?
G.EN.E.R.A. Centre for Reproductive Medicine (Italy)

When is the study starting and how long is it expected to run for?
December 2013 to December 2014

Who is funding the study?
G.EN.E.R.A. Centre for Reproductive Medicine (Italy)

Who is the main contact?
Dr Antonio Capalbo
capalbo@generaroma.it

Contact information

Type(s)
Scientific

Contact name
Dr Antonio Capalbo

Contact details
Via G. De Notaris 2/b
Rome
Italy
00197
+39 (0)63269791
capalbo@generaroma.it

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
GENERA0042013

Study information

Scientific Title
Influence of morphological grade and developmental rate on euploid blastocysts implantation potential: a non-selection prospective randomized controlled trial

Study objectives
A non-selection prospective randomised controlled trial to define the real influence of morphology and developmental rate of euploid blastocysts on ongoing implantation rate. Outcomes of morphologically different blastocysts transferred in intracytoplasmic sperm injection (ICSI) cycles of women undergoing preimplantation genetic screening (PGS) will be compared. Morphology will be evaluated accordingly to Gardner and Schoolcraft (1994) and blastocysts will be grouped into four classes (poor, average, good and excellent morphology). Also, developmental rate will be considered and blastocysts will be grouped into two classes (faster growing if reaching a stage compatible with biopsy on day 5 of embryo development, slower growing if reaching the same stage on day 6 or 7). According to the study hypothesis,

conventional parameters of blastocyst evaluation do not relate with implantation during euploid frozen blastocyst transfer cycles.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Local Medical Ethics Committee (Clinica Valle Giulia Ethics Committee), 01/12/2013, GENERA0042013_ethical approval

Study design
Non-selection randomized controlled trial

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Infertility in females undergoing PGS cycles

Interventions
The study would be structured as follows:
1. Ovarian stimulation by agonist or antagonist protocol
2. Ovum pick up performed 36 hours after human chorionic gonadotropin (HCG) administration
3. In vitro fertilization performed by intracytoplasmic sperm injection (ICSI)
4. In vitro culture performed with sequential media in 6% CO2 and 5% O2 atmosphere
5. Trophectoderm biopsy will be performed when the embryo will reach the expanded blastocyst stage. Blastocysts will be cryopreserved thereafter by vitrification, in order to perform the transfer in a thawing cycle
6. Blastocysts will be graded according to Gardner and Schoolcraft (1994)
7. Diagnosis will be performed through quantitative polymerase chain reaction (qPCR) by a referral center
8. In case more than one euploid blastocyst is found in the same cohort from a patient, the embryo to be thawed and transferred will be randomized on the day of transfer by an independent operator. If a patient produces a single euploid blastocyst, it will be directly transferred and included in the study.
9. Luteal support by Progesterone 200 mg vaginally three times a day from oocyte retrieval plus one day

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Ongoing implantation rate. It will be expressed as the number of blastocyst implanted (after 12 weeks) from the day of embryo transfer divided by the total number of blastocysts transferred. It will be updated up to 12 weeks from the last blastocyst transfer performed before the 01/12/2014.

Secondary outcome measures
1. Survival rate. It will be expressed as the number of surviving blastocysts after thawing divided by the total number of blastocysts thawed up to 01/12/2014.
2. Re-expansion rate within 3 hours post warming. It will be expressed as the number of blastocysts re-expanding within no more than 3 hours after thawing divided by the total number of blastocysts surviving to the warming procedure up to 01/12/2014.
3. Biochemical rate. It will be expressed as the number of transfers resulting in a β-hCG positive test without a proper clinical pregnancy divided by the total number of transfers resulting in a β-hCG positive test. It will be updated up to 2 weeks from the last blastocyst transfer performed before 01/12/2014.
4. Abortion rate. It will be expressed as the number of miscarriages divided by the total number of clinical pregnancies. It will be updated up to 12 weeks from the last blastocyst transfer performed before 01/12/2014.

Overall study start date
01/12/2013

Completion date
01/12/2014

Eligibility

Key inclusion criteria
1. All consecutive patients enrolled for blastocyst stage PGS cycles
2. Signed consent form

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
300 frozen single blastocyst transfer cycles

Key exclusion criteria
1. Positive serology for hepatitis B or C or HIV
2. Persisting ovarian cysts > 30 mm diameter
3. Patient is a carrier of monogenic diseases or chromosomal abnormalities
4. Known American Society for Reproductive Medicine (ASRM) Grade III or IV endometriosis
5. Maternal disease that is not clinically stable and known to impact the ability to become pregnant or carry a pregnancy to term
5.1. Lupus
5.2. Chronic liver or kidney disease
5.3. Body mass index (BMI) greater than 30
5.4. Uncontrolled hypertension
5.5. Anti-phospholipid antibody
5.6. Thrombophilia
5.7. Insulin-dependent diabetes

Date of first enrolment
01/12/2013

Date of final enrolment
01/12/2014

Locations

Countries of recruitment
Italy

Study participating centre
Genera Centre for Reproductive Medicine
Rome
Italy
00197

Sponsor information

Organisation
Genera Centre for Reproductive Medicine (Italy)

Sponsor details
Via G. De Notaris 2/b
Rome
Italy
00197
+39 (0)63269791
capalbo@generaroma.it

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05aq4y378

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
G.EN.E.R.A. Centre for Reproductive Medicine (Italy)

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