BRCA mutations and Ovarian ageing in women applying for in vitro fertilization and preimplantation genetiC diAgnosis

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON21616

Source
NTR

Brief title
BROCA-2

Health condition

BRCA1/2, ovarian reserve (AFC, AMH, ovarian response), ongoing pregnancy BRCA1/2, ovariele reserve (AFC, AMH, ovariele response), doorgaande zwangerschap

Sponsors and support

Primary sponsor: Participating sites: UMC Utrecht, Maastricht UMC+, Academic Hospital Brussels, UMC Groningen, Academic Medical Center Amsterdam
Source(s) of monetary or material Support: Self funding

Intervention

Outcome measures

Primary outcome

Serum AMH level

Secondary outcome

- AFC

- Amount of poor response (less than 4 oocytes at retrieval or cancellation due to insufficient follicle growths, i.e. < 4 dominant follicles sized ¡Ý14 mm growing)

- Number of retrieved oocytes (total amount and MII) after first cycle COH

- Ongoing and clinical pregnancy rate

Study description

Background summary

Rationale:

The study proposal aims to confirm the observation of a reduced quantity of the follicle pool in BRCA (Breast Cancer) mutation-positive women. If confirmed, advanced ovarian ageing in BRCA mutated women will have a major impact on their general health and fertility prospects. Furthermore, identification of genes that contribute to the endowment and wastage of follicles in the ovaries and thus timing of menopause will add to the understanding of the physiological mechanism of the ovarian ageing process.

In the current study we will be able to study the effect of BRCA mutations on the ovarian ageing process, by comparing serum anti-Müllerian hormone (AMH) levels between cohorts of BRCA mutation-positive women and normal controls, applying for in vitro fertilization (IVF) with preimplantation genetic diagnosis (PGD).

The main hypothesis is that normo-ovulatory women with a deleterious BRCA mutation have lower levels of AMH compared to normal controls, with at least a difference of 0.90 ng/ml, suggesting an effect size of approximately five years in menopausal age.

Objective:

To demonstrate the presence of a reduced age specific ovarian reserve status in BRCA mutation carriers by:

1.using serum AMH as ovarian reserve test

2.using the antral follicle count (AFC) as ovarian reserve test

3.using ovarian response to ovarian hyperstimulation for IVF as proxy variable of ovarian reserve status

Study design: The study is designed as an observational prospective cohort study in exposed and non-exposed women during their first IVF with ICSI and PGD treatment cycle

Study population: Couples, with normo-ovulatory women between 18 and 41 years old, applying for their first IVF with ICSI and PGD treatment cycle in view of their status as carrier of a female BRCA mutation will be asked to participate. Normo-ovulatory women between 18 and 41 years old, who visit the department of Reproductive Medicine for their first IVF, with ICSI and PGD treatment cycle unsuspected for reduced ovarian reserve, are asked to participate as control group.

Main study endpoints: The main study endpoint will be advanced ovarian ageing measured by serum AMH levels.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The nature and extent of the burden and risks associated with participation can be stated as negligible. Participating is not associated with (medical) benefits.

Study objective

The main hypothesis is that normo-ovulatory women with a deleterious BRCA mutation have lower levels of AMH compared to normal controls, with at least a difference of 0.90 ng/ml, suggesting an effect size of approximately five years in menopausal age.

Study design

The aim is to investigate a total of 34 BRCA mutation positive women and 91 controls in a period of approximately 4 years. Data analysis and publishing results will take ½ year, resulting in a total study duration of approximately 5 years.

Intervention

blood sample

Contacts

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Eligibility criteria

Inclusion criteria

Case group (BRCA mutation carriers)

- Female age > 18 years and < 40 years

- Regular menstrual cycles (i.e. mean cycle length of 21-35 days)

- First IVF with ICSI and PGD treatment cycle due to a female pathogenic BRCA mutation

- Written informed consent

Controle group (non suspected for BRCA mutation):

- Female age > 18 years and < 40 years

- Regular menstrual cycles (i.e. mean cycle length of 21-35 days)

- First IVF with ICSI and PGD treatment cycle due to an indication unsuspected for reduced ovarian reserve status

- Written informed consent

Exclusion criteria

Case group (BRCA mutation carriers)

- Ovarian surgery

- Chemo therapy

- Radiation therapy to the pelvis, lower abdomen or total body radiation

- Known female endocrine or autoimmune abnormalities (i.e. Cushing syndrome, type I Diabetes Mellitus, hypothyroidism, hyperprolactinemia, adrenal insufficiency, hypoparathyriodism, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)

- Body Mass Index > 35 kg/m2

- Polycystic Ovarian Syndrome (Rotterdam criteria)

- Early follicular FSH > 15 IU/L

- Known Human immunodeficiency virus (HIV) infection

- Known female genetic abnormalities suspected for subfertility (structural or numerical abnormalities of the X-chromosome (i.e. Turner¡¯s syndrome, fragile X syndrome), or abnormalities of human autosomal functionally relevant genes, other than a BRCA mutation, suspected for subfertility

Controle group (non suspected for BRCA mutation):

- Ovarian surgery

- Chemo therapy

- Radiation therapy to the pelvis, lower abdomen or total body radiation

- Known female endocrine or autoimmune abnormalities (i.e. Cushing syndrome, type I Diabetes Mellitus, hypothyroidism, hyperprolactinemia, adrenal insufficiency, hypoparathyriodism, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)

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Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2014
Enrollment:	125
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	25-07-2014
Application type:	First submission

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
NTR-new	NL4347
NTR-old	NTR4703
Other	UMC Utrecht : 14-175

Study results

Summary results
N/A