TUbectomy with delayed oophorectomy as alternative for risk-reducing salpingo-oophorectomy in BrcA-Women to assess the Safety of Prevention: the TUBA-WISP II study

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To evaluate RRS with delayed RRO as an alternative for RRSO in BRCA1/2 gene germline mutation carriers. We hypothesize that RRS with delayed RRO leads to an equal ovarian cancer incidence when compared to RRSO.

Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Obstetric and gynaecological therapeutic procedures
Study type	Interventional research applied for the first time in human subjects

Summary

ID

NL-OMON55319

Source
ToetsingOnline

Brief title
TUBA-WISP II

Condition

- Obstetric and gynaecological therapeutic procedures

Synonym
hereditary breast and ovarian cancer; BRCA mutation

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Collectebussenfonds

Intervention

- Surigical procedure

Keyword: BRCA, Oophorectomy, Risk-reducing, Salpingectomy

Explanation

N.a.

Outcome measures

Primary outcome

Primary study outcome is high grade serous (ovarian) cancer incidence at the
 age of 45 for BRCA1 and 50 for BRCA2 germline mutation carriers

Secondary outcome

Secondary endpoints are:
• High grade serous (ovarian) cancer incidence at the age of 70
• Incidence of (pre)malignant findings in tubes/ovaries
• Peri-operative morbidity and mortality
• Incidence of pelvic cancer (other than ovarian cancer)
• Breast cancer
• Uptake of risk reducing oophorectomy

Study description

Background summary

In BRCA 1/2 gene mutation carriers, a risk-reducing salpingo-oophorectomy (RRSO) is recommended around the age of 40. This recommendation is based on a 10-40% life-time risk of ovarian cancer in this population and disappointing results of ovarian cancer surveillance for early detection. Moreover, the mortality rate of ovarian cancer is high. Effects of RRSO are a decrease in ovarian cancer risk (80-96%) on one hand and immediate onset of menopause and non-cancer related morbidity on the other hand. The fifty percent breast cancer risk reduction after RRSO has become disputable in the last years. Based on

multiple studies showing that most high-grade serous ovarian cancers develop at the distal end of the Fallopian tube, an innovative strategy for RRSO has been developed for this study proposal: risk-reducing salpingectomy (RRS) with delayed risk-reducing oophorectomy (RRO). However, the safety of this strategy has not been proven yet. Before implementing this innovative strategy as standard care we need to investigate the long term effects on ovarian cancer incidence.

Study objective

To evaluate RRS with delayed RRO as an alternative for RRSO in BRCA1/2 gene germline mutation carriers. We hypothesize that RRS with delayed RRO leads to an equal ovarian cancer incidence when compared to RRSO.

Study design

A prospective preference study.

Intervention

Standard treatment: RRSO
o BRCA1 at a maximum age of 40 (advised between age 35 and 40)
o BRCA2 at a maximum age of 45 (advised between age 40 and 45)

Innovative treatment: RRS when childbearing is completed with delayed RRO
o BRCA1: RRS at age 25-40 and RRO at a maximum age of 45 (advised between 35 and 45).
o BRCA2: RRS at age 25-45 and RRO at a maximum age of 50 (advised between age 40 and 50).

Study burden and risks

Participants are followed via their treating physician. At the moment of inclusion, baseline characteristics will be reported to the study group. Within three months after surgery, pathological and surgical outcomes will be reported. During long-term follow up a biennial update will report on baseline demographics, ovarian cancer incidence, prophylactic breast surgery, incidence of non-ovarian pelvic cancer, breast cancer and surgery related morbidity. Biennial screening is not obligatory, the biennial update may be based upon a national pathology database. If women exceed the recommended age limit for oophorectomy, we recommend a yearly contact to monitor these women and reconsider the second surgery.
The most important risk for participants is the risk of developing ovarian cancer within the interval between RRS and RRO. We estimate that risk to be about 1-2% when RRO is postponed for five years in the scenario that the earlier salpingectomy does not reduce ovarian cancer risk at all. Furthermore,

in the innovative treatment, the participant will undergo laparoscopy twice.

Contacts

Scientific
Radboud Universitair Medisch Centrum
T.A. Gootzen
Geert Grooteplein Zuid 10
Nijmegen 6525 GA
Netherlands
0248186163
Public
Radboud Universitair Medisch Centrum
T.A. Gootzen
Geert Grooteplein Zuid 10
Nijmegen 6525 GA
Netherlands
0248186163

Trial sites

Trial sites in the Netherlands

Elisabeth-Tweesteden ziekenhuis
Target size: 50

Antoni van Leeuwenhoek (AVL)
Target size: 50

Universitair Medisch Centrum Groningen
Target size: 120

Medisch Centrum Leeuwarden (MCL)
Target size: 25

Maxima Medisch Centrum
Target size: 15

Isala
Target size: 20

Amphia Ziekenhuis
Target size: 15

Maastricht Universitair Medisch Centrum +
Target size: 80

Radboud Universitair Medisch Centrum
Target size: 250

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 150

Catharina-ziekenhuis
Target size: 30

Universitair Medisch Centrum Utrecht
Target size: 40

Leids Universitair Medisch Centrum
Target size: 35

Amsterdam UMC
Target size: 45

Medisch Spectrum Twente
Target size: 20

Listed location countries

Brazil, Netherlands, Germany, Belgium, Austria, Spain, Sweden, Italy, Mexico, Ireland, Norway, Uruguay, United States, Australia, Poland

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Women with a class 5 (definitely pathogenic) BRCA1 or BRCA2 germline mutation in one of the participating centers.
• Age at inclusion;
o BRCA1: 25-40 years
o BRCA2: 25-45 years
• Childbearing completed
• Presence of at least one fallopian tube

Exclusion criteria

• Postmenopausal status (natural menopause or due to treatment)
• Wish for second stage RRO within two years after RRS
• Legally incapable

• Prior bilateral salpingectomy
• A personal history of ovarian, fallopian tube or peritoneal cancer
• Current diagnosis or treatment for malignant disease

Study design

Design

Study phase:	N/A
Study type:	Interventional research applied for the first time in human subjects
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Other type of control
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	26-04-2020
Enrollment:	2000
Duration:	120 months (per patient)
Type:	Actual

WORLD

Recruitment status:	Recruitment started
Start date (anticipated):	01-01-2021
Enrollment:	3000
Type:	Actual

Medical products/devices used

Product type:	N.a.

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	18-12-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-01-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-02-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-02-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-07-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-01-2021
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-01-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-05-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-08-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-03-2025
Application type:	Amendment
Review commission:	METC Oost-Nederland

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
ClinicalTrials.gov	NCT04294927
CCMO	NL70691.091.19
Research portal	NL-006563