Prevention of breast cancer in high risk women by monitoring microrna expression in nipple aspirate fluid.

Published: 06-06-2006
Last updated: 15-05-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON44762

Source
ToetsingOnline

Brief title
MicroRNA expression in nipple aspirate fluid.

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders

Synonym
breast cancer, breast carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW,Vissers stichting;IKMN;KWF

Intervention

Keyword: Breast cancer, Methylation, Nipple aspiration, Screening

Outcome measures

Primary outcome

-Quantification of miRNA expression levels from nipple aspirate fluid samples

collected annually.

-Breast cancer development and their histological features.

-Establishing a biobank of blood samples (plasma and serum) of women at

increased breast cancer risk

Secondary outcome

-Discomfort, uncertainty and distress experienced because of and during

procedure

Study description

Background summary

Breast cancer develops by the stepwise accumulation of interacting epigenetic and genetic events over time. While genetic events are specific processes that differ greatly between patients, epigenetic events are more generally occurring in breast cancer development. Therefore, epigenetic monitoring (in addition to genetic monitoring) could be a breakthrough in breast cancer screening and prevention. Gene promoter hypermethylation has been described as a common epigenetic mechanism to silence tumor suppressor gene expression adding to breast cancer development. Another system that is currently considered to initiate and sustain epigenetic change is miRNAs. miRNAs are small non-protein-coding RNA molecules, which can play important regulatory roles in posttranscriptional gene expression.

In women at high risk, not all women will develop breast cancer. Diagnostically

there is a need for better procedures that will predict accurately who will and who will not develop breast cancer. In a previous study, we showed significant differences in methylation levels between NAF from cancerous breasts and NAF from healthy controls. Differences in methylation were however not large enough to warrant further studies to work towards a clinically useful test. This was especially true for the comparison between the affected and the non-affected breast of the same patient, which is of crucial relevance in view of our objective to implement NAF as a new screening method. Therefore, we aim to assess the occurrence and changes over time of microRNA expression patterns in nipple aspirate fluids of women at high risk for breast cancer to determine risks and correcting timing of interventions.

Furthermore, blood samples will be taken to identify biomarkers of breast cancer in blood.

Study objective

To establish biomarkers in nipple aspirate fluid, follow them in time and link them to breast cancer development at its earliest stage in women at high risk for breast cancer. Threshold values of biomarkers will be determined that point to a significant risk of imminent breast cancer development, thereby indicating the right time of prophylactic breast surgery in these high-risk women.

Study design

Annual nipple aspiration is performed on women at high (>20% lifetime) risk for breast cancer for ten years

A one time dose of 4 IE oxytocin nasal spray is adminstered prior to the nipple aspiration procedure. Nipple fluid is obtained through use of a vacuum system. In women at increased breast cancer risk blood will be collected (2 tubes for serum, 1 tube for plasma) to storage in the Biobank.

Study burden and risks

This project aims to set up a program to monitor development of molecular biomarker changes in nipple aspirate fluid to optimally time preventive breast surgery in women at high risk of developing breast cancer. The ultimate goal is to provide a new screening method in this high-risk population, with a > 20% life-time risk of developing breast cancer. This will allow on one hand postponing or avoiding a mutilating operation as much as possible (reducing morbidity), while on the other hand development of invasive breast cancer will be prevented (reducing mortality). Oxytocin-supported nipple fluid aspiration is very well tolerated as has been demonstrated in our previous study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Germline BRCA1 or BRCA2 mutation
- A > 20% lifetime risk of developing breast cancer
- Previous DCIS/invasive breast cancer

Exclusion criteria

-Bilateral ablative breast surgery
-Bilateral breast reduction with nipple graft
-Pregnancy or lactating
-Active breast infection

-Disseminated disease

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-08-2008
Enrollment:	720
Type:	Actual

Ethics review

Approved WMO Date:	06-06-2006
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	18-01-2008
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-11-2008
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-04-2010
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	16-02-2011
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-04-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-10-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-08-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-09-2017
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	24-06-2020
Application type:	Amendment
Review commission:	METC NedMec

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
CCMO	NL11690.041.06