The role of intestinal microbiota in breast cancer treatment with hormone therapy: a pathway to new therapeutic options

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Ethical review	Approved WMO
Status	Completed
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON53061

Source
ToetsingOnline

Brief title
Intestinal microbiota in breast cancer patients treated with hormonetherapy

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders

Synonym
Breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Breast cancer, Estrogen, Hormone therapy, Intestinal microbiota

Outcome measures

Primary outcome

The primary endpoints include, the microbiota composition before and during systemic hormone therapy. Further, microbiota composition in relation to systemic estrogen and endoxifen levels will be analysed.

Secondary outcome

Secondary endpoints include absolute microbiota abundance, ß-glucuronidase activity. Estrogen metabolites during tamoxifen therapy will be quantified. Furthermore, the CYP polymorphism will be quantified.

Study description

Background summary

Gut microbiota and host determinants evolve in symbiotic and dependent relationships resulting in a personal ecosystem. In case of dysbiosis, microbiota can instigate cancer development and even change response to systemic cancer treatment.
High circulating estrogen levels are recognized as a causal factor for estrogen receptor positive breast cancer development. Microbiota related estrogen sources are the estrobolome (the aggregate of bacterial genes capable of metabolizing estrogens) andbacterial ß-glucuronidase activity that increases the availability of intestinal estrogen for reabsorption into the bloodstream. Correlations between microbiota related estrogens and systemic estrogen levels are already proven. However, there*s no knowledge on the influence of microbiota composition in breast cancer treatment outcomes.
We hypothesize that microbiota and it's related ß-glucuronidase activity influences intestinal metabolism of tamoxifen*s and it's related metabolite, endoxifen.

Study objective

The main goal is to show in postmenopausal estrogen receptor positive breast cancer patients the influence of:
Microbiota composition and ß-glucuronidase activity on systemic endoxifen levels during tamoxifen therapy.

Study design

An explorative prospective observational multicenter cohort study will be conducted in Maastricht University Medical Center, Maxima Medical Center, Elkerliek Hospital, Catharina Hospital, and Admiraal de Ruyter Hospital.

After informed consent, patient and tumor characteristics will be gathered. Before and during hormone therapy, microbiota composition will be analyzed by mass spectrometry and 16S rRNA Next Generation Sequencing, and absolute abundance will be assessed through qPCR. Bacterial functional activity of ß-glucuronidase will be measured to determine its influence on tamoxifen metabolism and intestinal estrogen reabsorption. Blood estrogens and endoxifen metabolites will be quantified by ultra-high performance-liquid-chromatography-mass-spectrometry. Questionnaires on patient*s compliance will be provided.

Study burden and risks

Postmenopausal breast cancer patients will be informed and asked to participate in this study during their outpatient clinic visit by their physician (or their representative; nurse practitioner / specialised nurse). After the physician has provided initial information on the study, the researcher is asked to explain the study in more detail, if the patient requests. Next, the patient is asked whether the researcher can contact the patient after a minimum of 2 days, by phone or face to face, to further explain the study. This followed by the request to sign the informed consent (in duplicate) if the patient is willing to participate. The informed consent will be co-signed by one of the researchers. After informed consent, patients will undergo standard workup and diagnostic procedures and treatments, according to the Dutch guideline. Additional to standard treatment, fecal samples and questionnaires on patients* (baseline) characteristics and compliance will be collected before and during (after approximately 2 months) hormone therapy. Blood samples will only be collected during tamoxifen therapy. Patients will have the ability to collect their fecal samples and fill in the questionnaire up to 2 days before, during or after their hospital visits. It will take 5 minutes to fill in the questionnaire. All other procedures can take place during hospital visits. Taken all together, blood collection introduces a minimal burden to the patients.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Postmenopausal estrogen receptor positive breast cancer patients in curative setting starting with tamoxifen
• Willing and able to undergo all study procedures
• Signed informed consent

Exclusion criteria

• HER2+ breast cancer
• Metastatic disease (M+)
• Systemic therapy during previous month
• Prior therapeutic antibiotic use in last 3 months

• Physically or mentally incapable or incompetent to sign informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-10-2017
Enrollment:	66
Type:	Actual

Ethics review

Approved WMO Date:	30-08-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL61646.068.17