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

No registrations found.

| | |
|---|---|
| **Ethical review** | Not applicable |
| **Status** | Pending |
| **Health condition type** | - |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON20717

**Source**
NTR

**Brief title**
Microbiota in breast cancer and hormone treatment

**Health condition**

Breast Cancer - Borstkanker
Microbiota - Darmbacteriën
Estrogen - Oestrogeen
Hormone therapy - Hormonale therapie

### Sponsors and support

**Primary sponsor:** Maastricht University Medical Center (MUMC+)
**Source(s) of monetary or material Support:** fund = initiator = sponsor

### Intervention

### Outcome measures

**Primary outcome**

The primary endpoint is microbiota composition before and during (after 6 – 12 weeks) systemic hormone therapy in relation to systemic estrogen and endoxifen levels in respectively the cohort treated with aromatase inhibitors and tamoxifen.

**Secondary outcome**

Secondary endpoints include absolute microbiota abundance, ß-glucuronidase activity and estrogen metabolites before and during (after 6 – 12 weeks) systemic hormone therapy.

Other study parameters includes tumour grade, presence of genetic mutation, compliance score, performance score, MUST score, patient (abdominal) history and history of smoking, antibiotic use, contraceptive use, adverse events and serious adverse events.

# Study description

**Background summary**

Rationale:

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) and bacterial 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 aromatase-inhibitors will have lower efficacies in the presence of an abundant estrobolome and high ß-glucuronidase activity. It’s also unclear whether microbiota influences intestinal absorption of tamoxifen’s related metabolite, endoxifen.

Objective:

The main goal is to show in postmenopausal estrogen receptor positive breast cancer patients the influence of:

1. Microbiota composition and ß-glucuronidase activity on systemic estrogen levels during aromatase inhibitor therapy.

2. Microbiota composition on systemic endoxifen levels during tamoxifen therapy.

Study design:

Explorative prospective multicenter cohort study.

Study population:

Inclusion criteria: postmenopausal estrogen receptor positive breast cancer patients in curative setting starting with hormone therapy with either aromatase inhibitors or tamoxifen. Exclusion criteria: HER2+ breast cancer / metastatic disease / systemic therapy during previous month except tamoxifen/ prior therapeutic antibiotic use in last 3 months / physically or mentally incapable or incompetent to sign informed consent.

66 patients will be included in each cohort

Intervention:

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

Main study parameters/endpoints:

The primary endpoint is microbiota composition before and during systemic hormone therapy in relation to systemic estrogen and endoxifen levels in respectively the cohort treated with aromatase inhibitors and tamoxifen. Secondary endpoints include absolute microbiota abundance, ß-glucuronidase activity and estrogen metabolites before and during systemic hormone therapy.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Patients will be asked to participate during hospital visit or by phone. After 2 days or more the patients is asked face to face or by phone to sign informed consent in duplicate. After informed consent, patients will undergo standard workup and diagnostic procedures and treatments, according to the Dutch guideline. Additional to standard treatment, fecal samples, blood samples, and questionnaires on patients' (baseline) characteristics and compliance will be collected before and during hormone therapy after 6-12 weeks.

Blood samples will be collected before and during hormone therapy in all patients treated with aromatase inhibitors. In case of tamoxifen 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 or during regular hospital visits. It will take 5 minutes to fill in the questionnaire. All other procedures can take place during regular hospital visits. Taken all together, only the additional blood collection introduces a minimal burden to the patients.

### Study objective

We hypothesize that aromatase-inhibitors will have lower efficacies in the presence of an abundant estrobolome and high ß-glucuronidase activity. It's also unclear whether microbiota influences intestinal absorption of tamoxifen's related metabolite, endoxifen.

### Study design

Collection of fecal and blood samples:

T1: Before start of therapy

T2: During therapy (after 6 – 12 weeks)

### Intervention

No interventions

Observational study

## Contacts

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# Eligibility criteria

## Inclusion criteria

• Postmenopausal estrogen receptor positive breast cancer patients in curative setting starting with hormone therapy with either aromatase inhibitors or tamoxifen

• Willing and able to undergo all study procedures

• Signed informed consent

## Exclusion criteria

• HER2+ breast cancer

• Metastatic disease

• Systemic therapy during previous month, except tamoxifen

• Prior therapeutic antibiotic use in last 3 months

• Physically or mentally incapable or incompetent to sign informed consent

# Study design

## Design

| | |
|---|---|
| Study type: | Observational non invasive |
| Intervention model: | Parallel |
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-09-2017 |
| Enrollment: | 132 |
| Type: | Anticipated |

## IPD sharing statement

**Plan to share IPD:** Undecided

# Ethics review

Not applicable

| | |
|---|---|
| Application type: | Not applicable |

# 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 | NL6141 |
| NTR-old | NTR6296 |
| Other | METC AzM/UM : 172016 |

# Study results

### Summary results

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