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

Gepubliceerd: 13-04-2017 Laatst bijgewerkt: 13-12-2022

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…

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON20717

Bron
NTR

Verkorte titel
Microbiota in breast cancer and hormone treatment

Aandoening

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

Ondersteuning

Primaire sponsor: Maastricht University Medical Center (MUMC+)
Overige ondersteuning: fund = initiator = sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

Collection of fecal and blood samples:

T1: Before start of therapy

T2: During therapy (after 6 – 12 weeks)

Onderzoeksproduct en/of interventie

No interventions

Observational study

Contactpersonen

Publiek

Maastricht University Medical Center +, Department of Surgery

R Aarnoutse
P.O. box 5800

Maastricht 6202 AZ
The Netherlands
+31 (0)433-881558 / +316-82.01.91.05

Wetenschappelijk

Maastricht University Medical Center +, Department of Surgery

R Aarnoutse
P.O. box 5800

Maastricht 6202 AZ
The Netherlands
+31 (0)433-881558 / +316-82.01.91.05

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• 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

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-09-2017
Aantal proefpersonen:	132
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6141
NTR-old	NTR6296
Ander register	METC AzM/UM : 172016

Resultaten

Samenvatting resultaten

-