A single arm multicenter biomarker study determining the response to taxane-based chemotherapy in metastatic breast cancer patients with ESR1 mutations in cellfree DNA

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON25511

Source
NTR

Brief title
TAX-ESR1 study

Health condition

breast cancer, metastasis, ESR1 mutations, chemotherapy

Sponsors and support

Primary sponsor: Erasmus MC Cancer Institute, department of Medical Oncology
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Outcome measures

Primary outcome

To establish whether patients with ER-positive, HER2- negative MBC with an ESR1 mutation will benefit from taxane based chemotherapy, measured as progression free survival rate at 6 months.

Secondary outcome

- To assess whether the efficacy and outcome on taxane based chemotherapy differ between ESR1 mutated versus wild-type patients.

- To explore whether serial measurement of ESR1 mutations can predict survival and efficacy of chemotherapy in patients with ER-positive, HER2-negative MBC.

- To explore whether different activating ESR1 mutations (e.g. D538G and Y537S) display differences in efficacy on chemotherapy.

- To explore whether chemotherapy can result in loss of ESR1 mutations.

- To explore whether other gene variants are associated with outcome to taxane-based treatment.

Study description

Background summary

Endocrine treatment is the mainstay of treatment for ER- positive metastatic breast cancer (MBC). Unfortunately, 40% of patients have no clinical benefit from first-line endocrine therapy due to intrinsic resistance, whereas the remainder of patients initially responding will eventually develop resistance during therapy. Importantly, once the tumor develops resistance to endocrine therapy, the tumor becomes more aggressive, leading to a poor prognosis. Recently, mutations in the gene encoding ERá, ESR1, have attracted particular interest as a mechanism for endocrine resistance in MBC. Since the ESR1 mutated cells grow independently from estrogen, we hypothesize that these tumor cells have higher cell division rates and are therefore more sensitive to the anti-tumor effects from chemotherapy. If this is the case, ESR1 mutated patients would still benefit from chemotherapy, reflected in an improved PFS. Therefore, we present here a biomarker study to investigate whether ESR1 mutated patients could still benefit from taxane-based chemotherapy.

Study objective

We hypothesize that patients with detectable ESR1 mutations in cell-free DNA benefit from chemotherapy, resulting in improved PFS.

Study design

- Baseline

- 2 weeks

- 6 weeks

- 3 months

- 6 months: determination of response

- Progression

Intervention

Blood draw for cfDNA isolation (20mL) at baseline, during treatment, after treatment and at progression.

Contacts

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Eligibility criteria

Inclusion criteria

- Female metastatic breast cancer patients with ER-positive, HER2- negative primary tumors;

- Previous treatment with at least an aromatase inhibitor either in adjuvant and/or metastatic setting;

- Considered fit enough to receive taxane-based chemotherapy by the treating physician;

- Intention to start with either paclitaxel or docetaxel as first line treatment for metastatic breast cancer or as second line treatment if the time between completion of first line chemotherapy for metastatic breast cancer and inclusion is more than three years.

- Patient with measurable disease as defined per RECIST1.1 or bone only disease on recent standard work-up for MBC;

- WHO performance status 0-2

- Age > 18 years

Exclusion criteria

- Previous chemotherapy for metastatic disease; completed within three years before inclusion

- Patients with locally advanced disease, primary not amendable for resection or radiation therapy with curative intent;

3- (neo)adjuvant chemotherapy within 6 months prior to treatment start;

- Anti-hormonal treatment for breast cancer within one week prior to treatment start;

- Symptomatic CNS metastasis (the presence of at least one key symptom in combination with radiologic evidence (positive contrast-enhanced CT or MRI of the brain)

- Serious illness or medical unstable condition prohibiting adequate treatment and follow-up.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2017
Enrollment:	185
Type:	Anticipated

Ethics review

Positive opinion

Date:	11-06-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 46354
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7082

Register	ID
NTR-old	NTR7280
CCMO	NL62417.078.17
OMON	NL-OMON46354

Study results