Dissecting the pathways of endocrine and chemotherapy resistance in breast cancer:
A translational research project of the EORTC 10041/BIG 3-04 MINDACT clinical trial

No registrations found.

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

Summary

ID

NL-OMON25567

Source
NTR

Brief title
EORTC-1550-BCG The MINDACT Relapses Project

Health condition

Breast Cancer

Sponsors and support

Primary sponsor: EORTC
Source(s) of monetary or material Support: This research is supported by grants from the Breast Cancer Research Foundation (BCRF), Gillings Foundation and the EORTC Cancer Research Fund

Intervention

Outcome measures

Primary outcome

Methods:
• Massive Parallel Sequencing of primary and relapse
• Whole-genome DNA-sequencing to detect somatic copy numbers, rearrangements and mutations at a genome-wide level.
• Transcriptonne seqyencing to detect RNA expression at a genonne-wide level.
• Comparison of histology, grade, ER, PgR, HER2 and Ki67 status with the respective analysis results of the primary tumours using the same technologies as applied on the primary tumour samples performed at the MINDACT central pathology facility.
• Evaluation of blood circulating DNA by custom based Massive Parallel Sequencing.

Secondary outcome

Overall survival and any further disease progression

Study description

Background summary

The EORTC-1550-BCG MINDACT Relapses project, is a translational research project evaluating patients
enrolled in the MINDACT trial who relapse(d) or develop(ed) a second primary breast tumour at some
time point. As biopsy of the first site of disease recurrence (local, regional, distant or a new primary
breast tumours) constitutes a standard clinical practice in relapsed patients with breast cancer, we
foresee a two-step project design.
During the first step (retrospective), all centres that participated in the MINDACT will be asked if patients
who already relapsed underwent a biopsy of their first relapsed site. It is estimated that approximately
70% of these patients underwent a biopsy of their first relapse (local, regional, distant or new primary
breast cancer), but 50% of this material is expected not to be available due to several reasons (e.g. centre
or patient not interested to participate, tumour sample from the metastasis not suitable for further

research).
Evaluation planned on the collected material:
• Massive Parallel Sequencing of primary and relapse (local, regional, distant or new primary) breast
tumours:
• Whole-genome DNA-sequencing to detect somatic copy numbers, rearrangements and mutations
at a genome-wide level.
• Transcriptome sequencing to detect RNA expression at a genome-wide level.
• Comparison of histology, grade, ER, PgR, HER2 and Ki67 status with the respective analysis results of
the primary tumours using the same technologies as applied on the primary tumour samples again
performed at the MINDACT central pathology facility in the European Institute of Oncology (Instituto
Europeo di Oncologia, IEO), Milan, Italy.
As a second step but similarly to the retrospective cohort, the enrolment of prospective patients is
foreseen from patients with first or second site of relapse (local, regional, distant or second primary
breast tumours) as well as blood samples, along with clinical information (pattern of relapse, timing of
relapse after completion of adjuvant treatment and outcomes in subsequent treatments) from the
MINDACT patients who are still on follow-up and who may eventually relapse. The above mentioned
analyses (MPS, central pathology review) will be performed on the prospectively collected tissue and
blood samples as well.
Both steps can be run in parallel, i.e. simultaneously, to save time and resources.
For both steps, a new patient informed consent is required in addition to ethical approvals from the
countries of all the institutions that are willing to participate.

Study objective

Comparing the tumor tissue of patients with a breast cancer relapse to the tumor tissue of their primary breast cancer may help to identify mechanisms that are responsible for the relapse after exposure to anticancer agents, and thus further our understanding on the pathways of endocrine and chemotherapy resistance in breast cancer.

Study design

At study entry tissue samples of the tumor relapse and normal tissue (and in the prospective part a bloodsample) will be collected as well as clinical information on the time and type of relapse.

At each disease progression, clinical information and a new blood sample will be collected.

Intervention

N/A

Contacts

Public
Antoni van Leeuwenhoek ziekenhuis / Netherlands Cancer Institute
Josephine Lopes Cardozo

+31 20 512 9111
Scientific
Antoni van Leeuwenhoek ziekenhuis / Netherlands Cancer Institute
Josephine Lopes Cardozo

+31 20 512 9111

Eligibility criteria

Inclusion criteria

Retrospective part:
• Written informed consent of agreement for participating in the research project.
• Patients must have been enrolled in the MINDACT study and received randomized or non-randomized
treatment within the study, of any type and any duration, and have consented to future research or
are willing to provide consent for use of the primary tumour sample.
• Patients must have a local, regional or distant breast cancer relapse or new primary breast cancer
lesion and have undergone a bioptic/excision procedure of the new, not previously irradiated, lesion
as part of routine clinical practice before initiation of a subsequent line of systemic treatment (any
line).
• At least one Formalin-Fixed Paraffin-embedded (FFPE) tissue block or fresh-frozen tissue (FFT) from
the biopsy or from the resection specimen of the relapsed or new primary disease site, available for

translational research purposes.
• If blood or normal tissue is available in the hospital, it will be collected as well. For clarity, if normal
tissue is not available, patients remain eligible for the research project but will not be prioritized for
the molecular analysis.
• Biopsies of bone lesions are accepted if no other metastatic lesions are available.
• Patients with brain metastases are accepted if brain-tissue is provided through surgical excision as
part of the routine clinical practice.

MINDACT patients who participated in similar international (e.g. AURORA) or national programs (e.g.
SAFIR) and have Next Generation Sequencing (NGS) results available through these projects for the
primary and relapse tissue can still participate in the retrospective part by sending us any leftover
material from the relapse biopsy to perform new analysis or share the NGS reports with us, after
relevant agreement of the Steering Committee (or an equal governing body) of the respective project.

Prospective part:
• Written informed consent of agreement for participating in the research project.
• Patients must have been enrolled in the MINDACT study and received randomized or non-randomized
treatment within the study, of any type and any duration, and have consented to future research or
are willing to provide consent for use of the primary tumour sample.
• Patients must have a new diagnosis of local, regional or distant breast cancer relapse or new primary
breast cancer lesion based on physical, radiological and/or laboratory evaluation, and will undergo a
biopsy of this new, not previously irradiated, lesion as part of routine clinical practice.
• The biopsy of the local, regional or distant breast cancer relapse or new primary breast cancer lesion
must be conducted either at the initial diagnosis of the BC relapse or at the first disease progression
upon any line of systemic treatment received. Of note, the biopsy of the metastatic lesion must be
conducted before initiation of a subsequent line of systemic treatment.
• At least one FFPE tissue block or FFT from the biopsy or from the resection specimen of the relapsed
or new primary disease site, available for translational research purposes.
• If blood or normal tissue is available in the hospital, it will be collected as well. For clarity, if normal
tissue is not available, patients remain eligible for the research project but will not be

prioritized for
the molecular analysis.
• Biopsies of bone lesions are accepted if no other metastatic lesions are available.
• Patients with brain metastases are accepted if brain-tissue is provided through surgical excision as
part of the routine clinical practice.
• Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2.
• The patient agrees to provide blood samples at enrolment in the research project and at the time of
new disease progression.
• The patient is eligible if she has not received palliative radiotherapy at the site to be biopsied.
• Patients who participated in the retrospective part are allowed to participate in the prospective part
as long as there is another new breast cancer lesion (local, regional or distant relapse or new primary
breast tumour) identified which has not been irradiated previously that will be biopsied by the site.
The biopsy and blood draw should be performed prior to the start of next line of treatment.

MINDACT patients who participated in similar international (e.g. AURORA) or national programs (e.g.
SAFIR) and have Next Generation Sequencing (NGS) results available for the primary and relapse tissue through these projects can still participate in the prospective part once a new relapse or new primary, that can be easily biopsied per treating physician judgment, occurs.

Exclusion criteria

- No tissue (or only cytology) available of the relapsed site

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-08-2020
Enrollment:	123
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

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	NL8826
CCMO	NL74291.031.20

Study results