Towards patient tailored cancer treatment supported by molecular imaging
IMPACT: IMaging PAtients for Cancer drug selecTion - Metastatic Breast Cancer

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

Summary

ID

NL-OMON41527

Source
ToetsingOnline

Brief title
IMPACT breast

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
mammacarcinoma, metastatic breast cancer

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Alpe d□HuZes imaging grant from the Dutch Cancer Society

Intervention

Keyword: ER-receptor, HER2-receptor, Metastatic breast cancer, Molecular imaging

Outcome measures

Primary outcome

In patients with measurable disease: treatment response on CT at 8 weeks (day 56 ± 3), according to RECIST1.1 criteria (both per patient and per metastasis).

In patients with (non-measurable) bone metastases only, clinical response to treatment: progressive disease is defined as substantial worsening of overall complaints, meriting discontinuation of therapy. (Non-)response is related to baseline 18F-FES-PET and 89Zr-trastuzumab-PET (both per patient and per metastasis analysis); and 18F-FDG-PET at 2 weeks of treatment (both per patient and per metastasis analysis).

Secondary outcome

- The relation between progression free survival (PFS, defined as time from start of treatment until moment of documented tumor progression or death) to either positive or negative baseline 18F-FES-PET, 89Zr-trastuzumab-PET and 2 week 18F-FDG-PET.

- The relation between DNA sequencing and RNA expression analysis (including miRNA analysis) of the biopsy and venous blood samples to all molecular, imaging (standard and experimental) and clinical follow-up data (treatment

response and survival).

- The relation between miRNA analysis of the baseline biopsy and a venous blood sample at baseline, and all other molecular, imaging and clinical follow-up data.

- The relation between peptide profiling of new baseline biopsy and venous blood samples (baseline and day of standard response assessment) and all other molecular, imaging and clinical follow-up data.

- The assessment of molecular changes of primary biopsy, new baseline biopsy and (optional) biopsy taken during treatment and the relation to all other molecular, imaging and clinical follow up data.

- The relation between CTC count (including comparison of enrichment methods) and ER/HER2 status of CTCs at baseline and all molecular findings of the available biopsies (primary, baseline and, if feasible later biopsies) and venous blood samples, all imaging and clinical follow-up data.

- The assessment of circulating tumor DNA analysis at baseline, day of early 18F-FDG-PET and standard response assessment to the molecular findings of the available biopsies and venous blood samples, as well as to all imaging and clinical follow-up data.

- The relation between peptide profiling of the baseline biopsy and venous blood samples (baseline and day of standard response assessment), and all other molecular, imaging and clinical follow-up data.

- The relation between circulating miRNA analysis (baseline) and all other molecular, imaging and clinical follow-up data.

- The quantification of the cost-effectiveness of the experimental imaging

(baseline 18F-FES-PET and 89Zr-trastuzumab-PET; 2 week 18F-FDG-PET) as

described in paragraph 7.4.6.

- To assess impact of baseline biopsy procedure and baseline molecular imaging,

as well as quality of Life (QoL) before and during therapy.

Study description

Background summary

Current patient work-up, including conventional imaging and pathological assessment of just one single biopsy, might be insufficient to identify metastatic breast cancer patients, who possibly benefit from first-line anti-hormonal or anti-HER2 therapy. As receptor conversion of the tumor is found quite frequently and molecular heterogeneity can occur within one patient, up-to-date whole body information is necessary to determine estrogen receptor (ER) and/or human epidermal growth factor receptor 2 (HER2) receptor status and subsequently guide therapy decision. With molecular imaging via PET this information can be obtained in a non-invasive, patient friendly way. Furthermore, to improve and individualize treatment and be able to identify (new) drug targets and biomarkers, sampling of venous blood, circulating tumor cells (CTC) as well as circulating tumor DNA and molecular characterization of one metastasis at the beginning and, if feasible, of an additional biopsy during therapy, is necessary.

Study objective

The primary objective is to evaluate the clinical utility of experimental PET scans, in the setting of metastasized breast cancer (MBC) at first presentation.
Secondary objectives:
- The relation between progression free survival (PFS, defined as time from start of treatment until moment of documented tumor progression or death) to either positive or negative baseline 18F-FES-PET, 89Zr-trastuzumab-PET and 2 week 18F-FDG-PET.
- The relation between DNA sequencing and RNA expression analysis (including miRNA analysis) of the biopsy and venous blood samples to all molecular, imaging (standard and experimental) and clinical follow-up data (treatment response and survival).
- The relation between miRNA analysis of the baseline biopsy and a venous blood sample at baseline, and all other molecular, imaging and clinical follow-up data.

- The relation between peptide profiling of new baseline biopsy and venous blood samples (baseline and day of standard response assessment) and all other molecular, imaging and clinical follow-up data.
- The assessment of molecular changes of primary biopsy, new baseline biopsy and (optional) biopsy taken during treatment and the relation to all other molecular, imaging and clinical follow up data.
- To compare CTC enrichment approaches and relate CTC count and ER/HER2 status of CTCs at baseline to all molecular, imaging and clinical follow-up data.
- The assessment of circulating tumor DNA analysis at baseline, day of early 18F-FDG-PET and standard response assessment to the molecular findings of the available biopsies and venous blood samples, as well as to all imaging and clinical follow-up data.
- The relation between peptide profiling of the baseline biopsy and venous blood samples (baseline and day of standard response assessment), and all other molecular, imaging and clinical follow-up data.
- The relation between circulating miRNA analysis (baseline) and all other molecular, imaging and clinical follow-up data.
- The quantification of the cost-effectiveness of the experimental imaging (baseline 18F-FES-PET and 89Zr-trastuzumab-PET; 2 week 18F-FDG-PET) as described in paragraph 7.4.6.
- The assessment of impact of biopsy procedure and molecular imaging (both at baseline), as well as quality of life assessment before and during therapy.

Study design

This will be a multicenter prospective observational cohort study in non-rapidly progressive MBC patients eligible for first-line systemic therapy. 200 consecutive patients will be recruited in the VUMC, UMCN, ERASMUS MC and UMCG.
After successful eligibility screening, all patients will undergo i) a biopsy, according to standard clinical care, but with additional tissue gain for DNA sequencing, RNA expression analysis (including miRNA analysis) and peptide profiling, ii) investigational pre-treatment FES- and 89Zr-trastuzumab PET, iii) sampling of venous blood for routine assessments, 89Zr-activity measurements, for CTC analysis (baseline), circulating miRNA analysis (baseline), peptide profiling (baseline & day of standard response assessment), circulating tumor DNA analysis (baseline, day of early 18F-FDG-PET & day of standard response assessment), as well as for germline DNA collection (baseline). Subsequent treatment will be based on the routine biopsy and/or performed molecular imaging. QoL assessment will take place at baseline, 6-7 and 12 (+/-1) weeks after treatment start. Treatment response will be evaluated after 2 weeks as early response assessment (with 18F-FDG-PET) and routinely at 8 weeks (day 56 ± 3) after treatment start (with CT). If feasible, another biopsy for molecular analysis will be taken during therapy.

Study burden and risks

In this study the patients will optimally make 4 (maximum 5) extra visits to the hospital: Screening procedure (visit 1); 18F-FES-PET and 89Zr-trastuzumab tracer injection (visit 2, possibly on 2 following (working)days); 89Zr-trastuzumab-PET (visit 3); 18F-FDG-PET for early response monitoring (visit 4).
After staging (by standard clinical procedures and additional whole body molecular imaging) 3 treatment groups will be formed. All 3 treatment groups will potentially benefit from this study design due to a more correct selection of the treatment and/or an additional treatment option, which would have been withheld after conventional staging. The additional PET scans (18F-FES-PET, 89Zr-trastuzumab and 1x 18F-FGD-PET) implement a radiation burden of about 31 mSv including the low dose CT for attenuation correction. This radiation burden is justifiable in this category of patients with metastatic cancer, by the information that can be obtained from this study, which will have direct consequences for diagnostic and therapeutic decision-making. Patients may experience side effects of the new tracers. Until now no side effects of 18F-FES have been registered. Three times, a side effect in terms of a hypersensitivity reaction has been observed using 89Zr-trastuzumab. Appropriate precautions have been taken to reduce the risk of such an event. The risk of (additional) tumor biopsies is considered low with a small risk on significant/major complications (0 to 1.6%) or death (0 to 0.48%). The risk of blood draws for molecular analysis is considered negligible. As the methodology of DNA sequencing, RNA profiling (including miRNA analysis), peptide profiling, CTC and circulating tumor DNA analysis is experimental, we are currently unsure about the potential benefit patients can derive from this information and we clearly emphasize the experimental nature of this part of the protocol.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patient with first presentation of MBC, regardless of ER and HER2 status of the primary tumor, who is eligible for first-line systemic therapy.
- Patient with non-rapidly progressive MBC, not requiring urgent initiation of chemotherapy, based on clinician's evaluation
- Patients in whom standard imaging work-up of MBC was recently (<= 28 days) performed
- Patient with measurable or clinically evaluable (bone only) disease on recent standard work up of MBC are eligible.
- Metastatic lesion(s) of which a histological biopsy can safely be obtained according to standard clinical care procedures.
- Performance score 0-2

Exclusion criteria

- Contraindications for systemic treatment (as will be assigned based on biopsy and experimental scan results), either chemotherapy, hormonal therapy or anti-HER2 therapy, based on clinical judgment of treating medical oncologist and patient history.
- Pregnant or lactating women.
- Rapidly progressive (visceral) disease requiring rapid initiation of chemotherapy.

Study design

Design

Study phase: 2

Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-08-2013
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-03-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-03-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	03-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-11-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2013-000551-41-NL
ClinicalTrials.gov	NCT01957332
CCMO	NL43582.042.13