Tumorresponse monitoring in patients with breast cancer treated with primary systemic therapy: Towards predicting response in both the primary tumor and in axillary lymph nodes

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

Summary

ID

NL-OMON31961

Source
ToetsingOnline

Brief title
Tumorresponse monitoring of primary systemic therapy

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: CTMM project in samenwerking met o.a. Philips,Philips

Intervention

Keyword: breastcancer, FDG-PET, primary systemic therapie, response monitoring

Outcome measures

Primary outcome

Sensitivity and specificity of FDG PET and MRI to assess early tumour response

of the primary tumour

Sensitivity and specificity of FDG PET/CT and seed localisation in measuring

(early) tumour response of the axilla.

Secondary outcome

not applicable

Study description

Background summary

The use of primary systemic therapy, or neoadjuvant chemotherapy, has gained an important role in the treatment of breast cancer. Systemic therapy before surgery has several advantages.

Firstly, the rate of breast-conserving surgery is increased after primary systemic therapy, because of reduction of tumorload. In a meta-analysis, Mauri et al. describe an increase in breast conserving surgery of 18%. A slightly increased risk of local recurrence was found. However, these recurrences mainly occurred in patients with clinically complete remission who only received irradiation to the breast without surgical treatment.
Secondly, the tumor response to systemic therapy can be evaluated enabling translational research which gives us more insight in the behavior of different tumor subtypes Interim radiological evaluation during primary systemic therapy creates the opportunity to switch to another regimen in case of unfavorable

response. The final tumor response remains based on pathological assessment after surgery.
The ultimate goal of primary systemic therapy is to improve survival. However, the advantage in survival after primary systemic therapy compared to adjuvant systemic therapy remains to be proven. Patients with a pathological complete remission after primary systemic therapy do have a better disease-free survival than patients with incomplete remission.5 Also, several trials comparing different chemotherapy regimes in a primary setting show a survival benefit for the superior regimen.

Response monitoring of the primary tumor
Response monitoring is a crucial process in the neoadjuvant setting. It is needed to select patients eligible for breast conserving therapies and to distinguish between favourable and unfavourable response. It provides the opportunity to switch the chemotherapy regimen in insufficiently responding tumors at an early time point.

Response monitoring of lymph node metastasis
Axillary pCR is described in 22-38% of patients treated with primary systemic therapy.15;16 Currently, this group of patients undergoes an axillary lymph node dissection, which was not necessary on retrospect. Although there is substantial similarity between axillary tumor response and response of the primary tumor, this correlation is too weak to reliably predict axillary tumor response solely based on primary tumor response. A reliable method to evaluate the axillary tumor response is however essential in order to reduce the rate of unnecessary ALND*s, without compromising oncological safety. We hypothesize that including PET/CT imaging in response monitoring of breast and axilla could help with identifying the patients that obtain a (near) pCR of the axilla, thus identifying patients in which axillary lymph node dissection can be omitted. In addition to response monitoring by PET we also propose a new method to evaluate axillary tumor response. With this method, a proven positive lymph node is marked prior to primary systemic therapy in order to obtain histopathological proof of response. After primary systemic therapy, the marked lymph node is removed for analysis. Based on pathological assessment of the tumor response in the marked lymph node, a decision can be made whether to perform an ALND or not.

Study objective

The aim of this protocol is twofold.
• Firstly, we aim to combine the new response monitoring method (PET imaging) with the present technique (dynamic CI-MRI imaging) in order to discriminate between favourable and unfavourable response of the primary tumor during and after neoadjuvant chemotherapy.
• Secondly, we aim to investigate whether the axillary tumor response to primary systemic therapy can be reliably assessed.

Study design

Two types of patients, scheduled to receive primary systemic therapy according to the N04POM trial, TRAIN trial and in the future the TIP trial, will be included in this study:
1. cN0: patients with negative axillary ultrasound findings and an unknown pathological nodal status.
2. cN+: patients with tumor positive cytology after FNA.

In the current protocol for neoadjuvant systemic treatment, dynamic CE-MRI imaging is included for response monitoring of the primary tumor and these findings will now be combined with the PET findings. All patients will receive 3 FDG/PET scans. Time point of the scans will be dependent on the type of chemotherapy regimen and HER2 expression:

In Her2 negative patients, treated with an antracycline or taxane based regimen:
• One FDG-PET at baseline, before primary systemic therapy, together with MRI
• One FDG-PET after 1 cycle of primary systemic therapy
• One FDG-PET after 3 cycles of primary systemic therapy, together with MRI

In Her2 positive patients, treated with a weekly trastuzumab based regimen:
• One FDG-PET at baseline, before primary systemic therapy, together with MRI
• One FDG-PET after 3 cycles of primary systemic therapy
• One FDG-PET after 8 cycles of primary systemic therapy, together with MRI

In the group of cN+ patients, axillary tumor response will be evaluated also by Radioactive seed localization (RSL). The tumor positive axillary lymph node will be marked prior to primary systemic therapy. In the same session of surgery for the breast tumor after systemic therapy, the marked lymph node will be detected using a gamma-ray detection probeand selectively removed. After removal of the marked lymph node, an ALND will be performed. The correlation between the tumor response in the marked lymph node and tumor response in the ALND specimen will be investigated.

Study burden and risks

Patients will receive three additional imaging examinations, namely three times a FDG-PET scan. Furthermore, I-125 seeds will be placed in a suspect lymph nodes in cN1 patients with a low risk on inflammation.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion in one of the clinical protocols that are part of the NKI-AVL neoadjuvant therapy program; women with breastcancer > 3 cm and/or axillary lymph node metastasis

Exclusion criteria

Exclusion in one of the clinical protocols that are part of the NKI-AVL neoadjuvant therapy program; Pregnancy or breastfeeding

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2008
Enrollment:	300
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 21498
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL23017.031.08
OMON	NL-OMON21498