SPectroscopic Assessment of Chemotherapy Efficacy in breast cancer patients

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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-OMON47637

Source
ToetsingOnline

Brief title
SPACE

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders

Synonym
breast cancer, breast neoplasm

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,Alpe d'HuZes / KWF

program grant

Intervention

Keyword: 7 Tesla MRI, Breast cancer, Monitoring neoadjuvant chemotherapy, Non-invasive

Outcome measures

Primary outcome

Phosphomonoester (PME) / Phosphodiester (PDE) or alternatively PME / inorganic phospor (Pi) signal ratios, prior to, and after the first cycle of chemotherapy as obtained from 31P-MRS as a function of pathologic non-response and positive lymph nodes.

Secondary outcome

Secondary study parameters as measured with (DCE-MRI, DWI, CEST-MRI) of the tumor prior to chemotherapy and after the first cycle of chemotherapy:

- DCE-MRI: Ktrans and kep values;

- DWI: ADC values;

- CEST-MRI: magnetisation transfer ratio (MTR) values.

Study description

Background summary

Neoadjuvant chemotherapy (NAC) before surgery is used in patients with aggressive breast cancer to reduce tumor volume and the risk of distant metastases. Unfortunately, the effect of neoadjuvant chemotherapy can only be assessed in a late phase of the therapy. Therefore, in case of an ineffective therapy, patients already suffered from the side effects of chemotherapy without any benefit. Currently, no good non-invasive method capable of assessing the efficacy of chemotherapy before the surgery is available. By using new non-invasive magnetic resonance imaging techniques we are able to evaluate tumor metabolism (by means of 31P-magnetic resonance spectroscopy (31P-MRS)). An ongoing feasibility study already showed differences in five

patients when the biomarkers are measured before and halfway the chemotherapy (11-146 / NL36429.041.11). To validate this biomarker to predict the response to NAC, more patients are needed. Furthermore, we are able to evaluate indirectly the vascularity (dynamic contrast-enhanced magnetic resonance imaging (with DCE-MRI)), cell density (with diffusion weighted imaging (DWI)) and the chemical exchange (with chemical exchange saturation transfer (CEST-MRI)). If we are able to prove that biomarkers based on MRI measurements that are assessed at the start of chemotherapy are able to select patients that will not respond to therapy, we can prevent those patients from receiving more of the ineffective neoadjuvant chemotherapy. The patient will not have to endure the side effects of ineffective neoadjuvant chemotherapy, which have a large impact on the quality of life of the patient and her direct environment. Applying metabolic imaging will be a step ahead towards personalized cancer care. It will provide more detailed information about the cancer, enabling tuning of the therapy to the individual patient. If this method works in this group of breast cancer patients it can be transferred to patients with other types of cancer who receive neoadjuvant chemotherapy. Moreover, a non-invasive method to assess metabolic changes directly in the cancer will also speed up development of new systemic therapies as its effects can be assessed in an early stage.

Study objective

First, the threshold for the biomarkers of 31P-MRS will be determined. These biomarkers can indicate whether a patient with breast cancer benefit from the neoadjuvant chemotherapy (NAC). Then it is determined whether a (combination of) biomarker(s) of DCE-MRI, DWI and CEST-MRI with and without 31P-MRS, also leads to a threshold value that indicates whether a patient with breast cancer will benefit from the NAC.

Study design

Prospective cohort study.

Study burden and risks

Subjects do not directly benefit from participation. Ultimately, in case of a positive outcome, future patients may benefit from a 7 Tesla (T) MRI scan. The added risks of study participation are considered negligible. Standardized 7T MRI checklists will be in effect to ensure MRI safety. The burden for the patient includes the time the patient will spend for making the extra 7T MRI scans. Patients will be compensated for travel costs because of the extra visits to the hospital for making the 7T MRI scan. Treatment of patients will be based on the standard, evidence based, medical care and will not be influenced by the DWI, CEST or 31P-MRS results of the 7T MRI scans or the

assessments of the pathological marker for tumor proliferation (Ki-67).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- 18 years or older;
- Female breast cancer patients selected for neoadjuvant chemotherapy;
- Stage Ic (max. 3 cm retromammilair, min. B cup size), II and III tumors.

Exclusion criteria

- Any prior surgery or radiotherapy for malignancy to the ipsilateral breast;

- Prior chemotherapy within 1 year;
- Karnofsky score of 70 or less;
- Pregnant or lactating women;
- Contra-indications to MRI scanning according to hospitals 7T MRI screening guideline of the UMC Utrecht or the AMC;
- Contraindications to administration of gadolinium-based contrast agent, including: prior allergic reaction to a gadolinium-based contrast agent and/or renal failure (defined as GFR < 30mL/min/1,73m2).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-11-2014
Enrollment:	76
Type:	Actual

Ethics review

Approved WMO Date:	16-10-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-04-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	16-07-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	METC NedMec

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
CCMO	NL49333.041.14