Liquid biopsies and imaging

Published: 23-08-2019
Last updated: 09-04-2024

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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-OMON52473

Source
ToetsingOnline

Brief title
LIMA

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Horizon 2020

Intervention

Keyword: Breast Cancer, Imaging, Liquid biopsy, Response Prediction

Outcome measures

Primary outcome

The primary end point is Residual Breast Cancer Burden in surgical excision specimen.

Secondary outcome

Secondary endpoints are radiological lesion volume on DCE MRI after NAC. In addition, ypT0/ypN0 (i.e., absence of invasive cancer and in-situ cancer in the breast and axillary nodes), ypT0/is ypN0 (i.e., absence of invasive cancer in the breast and axillary nodes, irrespective of ductal carcinoma in situ), and ypT0/is (i.e., absence of invasive cancer in the breast irrespective of ductal carcinoma in situ or nodal involvement).

Study description

Background summary

It is currently impossible to predict which individual breast cancers will respond sufficiently to chemotherapy and which will not. Neoadjuvant chemotherapy (NAC) switches the order of the treatment: the chemotherapy is given first - prior to surgery - allowing tumor response to be monitored while the cancer is still in-situ. This treatment schedule also offers the possibility to switch treatment upon demonstration of lack of response. Ideally this should be done at the earliest signs of failure to treatment, to prevent unnecessary exposure of patients to ineffective and often toxic chemotherapy. Conversely, NAC may allow drug therapy to be stopped early when a complete response has been achieved or if the disease becomes progressive. Anatomical breast imaging is the standard method to assess response. However, it is well known that in individual patients, changes in tumor size have limited efficacy to predict the ultimate response after treatment. Whereas monitoring the biological properties of the cancer using functional imaging may provide complementary information, imaging can only visualize macroscopic disease. Recent studies have suggested there is an inverse relation between the level of circulating tumor cells and/or DNA fragments of tumor cells in the blood and the response to chemotherapy, making this a potentially powerful tool in

predicting tumor response on a microscopic level, while also representing tumor heterogeneity. We therefore hypothesize that a combination of known clinicopathological factors, (functional) imaging and analysis of blood (circulating tumor cells and tumor DNA) during NAC can reliably predict the residual breast cancer burden after NAC in individual breast cancer patients.

Study objective

The primary objective is to demonstrate proof of concept by exploring to what extent combinations of clinicipathological factors, multispectral magnetic resonance imaging (MRI), and liquid biopsies prior to, during and after completion of NAC, are able to forecast residual cancer burden after NAC in addition to conventional clinical and pathological information.

Study design

Prospective observational cohort study

Study burden and risks

Patients in our study will undergo three MRI scans: before start of NAC, halfway through and after completion of NAC. For some patients, this may mean one additional MRI scan relative to routine clinical care, some patients would undergo 3 MRI scans in routine clinical care. All patients will undergo a PET/CT scan before the start of NAC. For a large portion of patients, this is part of routine clinical care. For a subset, this will be for the purpose of the study.
In addition, a blood draw of 30ml will be taken every first day of the chemotherapy cycle. The blood draw will take place on a moment where a blood draw or iv placement is planned, so the patients don*t have to undergo additional venipuncture. The study entails no additional site visits, physical examination, surveys or tests, apart from the before mentioned procedures. Patients are expected to experience minimal burden and have negligible risk. Allergic reaction to MRI contrast agent may occur in rare cases. Potential benefits may be better staging by a PET/CT, and improved response evaluation by an additional MRI.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX

NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Female patients aged 18 years or older
- Histologically proven invasive breast carcinoma
- Planned for neoadjuvant chemotherapy (and in case of a Her2-positive tumor: addition of trastuzumab and/or pertuzumab)

Exclusion criteria

- ER-positive, HER2-negative, B&R grade 1 breast cancer
- Inflammatory breast cancer
- Distant metastases on PET/CT
- Ipsilateral breast cancer in history (contralateral breast cancer >5 years ago is allowed)
- Other active malignant disease in the past 5 years (excluded squamous cell or basal cell carcinoma of the skin)
- Pregnant or lactating women.
- Contra-indications for MRI according to standard hospital guidelines.
- Contra-indications for gadolinium-based contrast-agent, including known prior allergic reaction to any contrastagent, and renal failure, defined by GFR < 30 mL/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):	17-12-2020
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	23-08-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-11-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	17-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2022
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	NL67308.041.19