Non-invasive nodal staging in breast cancer with MRI Lymphography using gadofosveset.

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

Summary

ID

NL-OMON43763

Source
ToetsingOnline

Brief title
Gadofosveset in breastlesions

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast cancer, Lymph node metastases

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Carla Boetes Fonds en Kankeronderzoekfonds Limburg

Intervention

Keyword: Breast Cancer, Gadofosveset, MRI, Sentinel Lymph node

Outcome measures

Primary outcome

The main study parameter will be the accuracy (sensitivity, specificity, NPV

and PPV) of the MRL in predicting the

involvement of metastases in the investigated lymph nodes. We will compare the

results of the MRL with the pathological

results of a negative SLNB or the ALND.

In cases with a positive MRL and negative SLNB, we will investigate if the MRL

is really wrong, or that we probably found

a case of a false negative SNLB procedure.

Secondary outcome

n.a.

Study description

Background summary

Lymph node status is one of the most important prognostic factors in breast cancer and is of particular value in choosing adjuvant therapy. About 30% of breast cancer patients have histopathologically positive axillary lymph nodes.
Nowadays, all breast cancer patients undergo a mammography, breast ultrasound, histology, and a breast MRI. After the diagnosis breast cancer has been determined, the current nodal staging consists of an axillary ultrasound and possible cytologic or histologic punction followed by sentinel lymph node biopsy (SLNB) and/or an axillary lymph node dissection (ALND). After introduction of the MRL, first the accuracy has to be established. If MRL is equally accurate to the current

nodal staging workup, skipping partly the SLNB and its histology might make this workup more efficient. So, accuracy will be researched by comparing the current, invasive, nodal-staging with noninvasive MRL in relation to the golden standard, histological examination of the SLNB and/or ALND.
In addition, MRL might be able to detect extra-axillary lymph node metastases which could induce a change in treatment
regimen for an unknown number of patients. Studies on a positive parasternal SLNB show a change in adjuvant treatment
in 0.9% of the patients. Furthermore, it is known that the SLNB has a false negative rate of 9.8%. In this pilot study we will
only investigate the axillary region with MRL. We know that a possible reason for a false negative SNLB is a low number
of specimens removed during the SLNB procedure. MRL might be able to detect the nodes missed by SLNB.

Study objective

The aim of this pilot-study is to examine the accuracy of MRL compared to current nodal staging methods. We expect an
acceptable accuracy of the MRL based on earlier studies with gadofosveset enhanced MRI in rectum cancer patients. Then the MRL could indicate a tailored made treatment possible. It is unlikely that the MRL can replace all SLNB*s considering the fact that it might not be able to detect nodal metastases smaller than 0.2mm. Detection of these metastases is crucial since they change adjuvant treatment regimen.

Study design

This study is designed as a single-center prospective cohort study. We plan to include 160 patients in this pilot-study.
Patients will be recruited in the Maastricht Universitair Medisch Centrum (MUMC). We expect a period needed to recruit of 15 months.
Patients will undergo an axillary MRI with gadofosveset contrast agent. With the MRI and coils used in this study we only investigate the axilla on the site of the breast cancer.
The accuracy of MRL will be determined on the basis of a node-to-node matching of imaged nodes to the definitive
histopathology. The pathologic examination of the SNLB or ALND will be regarded as the golden standard for nodal
involvement. The pathologic examination will take place following the regular procedure. During microscopic examination each node will
be recorded as benign, or isolated tumor cell (ITC) (pN0(i+)) (* 0.2mm), or micrometastase (pN1mi) (0.2 * 2.0mm) or
macrometastase (pN1) (>2.0mm).
Overall nodal status will be reported following the regular procedure. With this result we can make the patient by patient

analysis.
The results of the pathologic examinations will be compared to the results of the MRL. The MRL will be assessed by two
radiologists, who will independently read all the images and they are blinded for earlier investigations. In the meantime
they will receive feedback about the pathologic results, in order to make a learning curve possible.
Each lymph node visible on MRL will be scored as benign or malignant using a confidence level score (0= definitely
benign, 1= probably benign, 2= possibly benign, 3= probably malignant, and 4= definitely malignant). Criteria for
malignancy on gadofosveset-MRI will be low signal intensity and absence of a *relief* sign.
The diagnostic performance of gadofosveset-MRI will be analyzed on lesion by lesion basis and on patient by patient
basis. In this way we can obtain precise validation of imaging findings with the underlying histopathology. The lesion by
lesion results will be translated to a patient by patient validation in order to obtain a clinically more relevant assessment of
the diagnostic performance on a patient basis.

Intervention

MRI of the lymph nodes in the axilla with gadofosveset contrast agent.

Study burden and risks

The patient who participates in this study will undergo all regular investigations to come to a proper staging of the breast
cancer. The current procedure on staging of breast cancer patients is extensive. The procedure includes in most cases a
MRI scan of the breast. For this study we will perform an extra MRI with gadofosveset contrast agent of the axilla a couple of days after the initial MRI scan. Further investigation needed for this study will not extra burdensome the patients, because all further procedures are already included in the regular treatment.

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

1. Female patient with histopathologically confirmed breast cancer about to undergo nodal staging.
2. Willing and able to undergo all study procedures
3. Has personally provided written informed consent;Additional inclusion criteria for 2nd axilla-MRI
1. Patient treated with neo-adjuvant therapy
2. Indication for ALND after neo-adjuvant therapy as result of regular treatment

Exclusion criteria

1. Age <18
2. Pregnancy
3. Contra indications for MRI such as pacemaker, aneurysm clips or severe claustrophobia.
4. Allergy to any of the ingredients of Gadofosveset (Ablavar®)
5. Being unable to give informed consent in person
6. Acute or chronic severe renal insufficiency (glomerular filtration rate < 45mL/min/1.73m2)
7. Acute renal insufficiency of any severity due to the hepato-renal syndrome
8. Known (or suspicion of) QT- prolongation

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-08-2012
Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ablavar
Generic name:	Gadofosveset Trisodium

Ethics review

Approved WMO

Date:	30-05-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	08-06-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	12-06-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-04-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2012-001174-29-NL
CCMO	NL40064.068.12

Study results

Date completed:	06-05-2016
Actual enrolment:	97

Summary results
Trial ended prematurely