Primary Radioactive Iodine Seed localisation in the Axilla in axillary node positive breast cancer combined with Sentinel node procedure (RISAS) following neoadjuvant chemotherapy (NAC): a novel surgical approach to accurately assess axillary response to neoadjuvant systemic therapy, thereby reducing future need for completion axillary lymph node dissection and subsequent morbidity

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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-OMON47808

Source
ToetsingOnline

Brief title
RISAS procedure in node positive breast cancer following NAC

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast therapeutic procedures

Synonym
lymph node metastasis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: KWF/Alpe d'Huzes foundation

Intervention

Keyword: Axillary lymph nodes, Breast cancer, Complete response, Neoadjuvant chemotherapy

Outcome measures

Primary outcome

The main goal of this study is to examine the accuracy (identification rate, sensitivity, NPV and FNR) of the RISAS procedure to identify axillary pCR, compared to the current axillary surgical procedure ALND. The pathologic examination of the ALND is the gold standard for nodal involvement and staging.

If the RISAS procedure is accurate in the evaluation of axillary pCR, this can result in reducing an ALND in these patients, thereby reducing the risk of developing potential morbidity of axillary surgery.

Secondary outcome

The secondary objective of this study is to examine the accuracy (identification rate, sensitivity, NPV and FNR) of both techniques used in

RISAS separately (i.e. SLNB and MARI), compared to ALND. Again, the pathologic examination of the ALND will be regarded as the gold standard for nodal involvement and staging.

Subgroup analyses might demonstrate that the use of a single technique is sufficiently accurate to identify axillary pCR in certain subgroups, indicating these patients only require either SLNB or MARI.

Study description

Background summary

Chemotherapy in clinically node positive breast cancer patients is increasingly administrated in a neoadjuvant setting. The standard treatment regimen in these cases is then: neoadjuvant chemotherapy (NAC) followed by breast surgery and an axillary lymph node dissection (ALND). NAC results in axillary pathologic complete response (pCR) in 1 out of 3 patients, indicating a complete absence of axillary metastases after completion of NAC. In such events, ALND can be regarded as overtreatment that creates unnecessary morbidity. Less invasive axillary surgery which can accurately assess axillary pCR is therefore preferred over standard ALND in all patients. In case of detection of remaining axillary lymph node metastases by this less invasive axillary surgical procedure, completion axillary treatment is standard of care.
The novel RISAS procedure is introduced as a possible less invasive axillary staging procedure. RISAS procedure contains Radioactive Iodine Seed localisation in the Axilla in axillary node positive breast cancer combined with a Sentinel node procedure.

Study objective

The main goal of this study is to examine the accuracy (identification rate of the MARI-node and Sentinel node, sensitivity, negative predictive value (NPV) and false-negative rate (FNR)) of the RISAS procedure compared to the current standard axillary lymph node dissection in clinically node positive breast cancer patients, treated with NAC.

Study design

The study is designed as an open-single arm multicenter intervention study. In this study 248 patients will be included during a 2 year period. Patients will be recruited in:
- Academic Breast Cancer Centre, Erasmus MC, Rotterdam
- Amphia Hospital, Breda
- Maastricht University Medical Centre, Maastricht
- University Medical Centre Utrecht, Utrecht

For this study, it is required that each participating hospital is already using I-125 seed placement to localize the primary tumor in breast cancer patients. As a consequence, all participating surgical oncologists are experienced with the use of I-125 seeds.

a) The RISAS-procedure consists of: insertion of an I-125 seed in a positive axillary lymph node, prior to the start of NAC. The I-125 seed will be placed simultaneously with the standard I-125 localisation procedure of the breast tumor which precludes extra visits. In case of several suspicious nodes on ultrasound, confirmed by pathology, the I-125 seed will be placed in the most suspicious node.
b) sentinel lymph node biopsy (SLNB): this procedure is a standard technique in clinically node negative breast cancer.

During definitive axillary surgery, the ALND is preceded by both selective excisions of the MARI-node as well as the dual tracer sentinel node(s). It may occur that both procedures converge in the same axillary lymph node.

Intervention

Prior to start of NAC, an I-125 seed will be placed in the pathologically confirmed axillary lymph node metastasis. After completion of NAC, all patients will undergo a RISAS procedure followed by ALND in a one-step surgical procedure.

Study burden and risks

Patients will undergo standard workup and diagnostic procedures and treatments, according to the Dutch guideline. For this study the RISAS procedure will be performed, preceding the axillary surgery (i.e. ALND). The RISAS procedure includes:
a) insertion of an I-125 seed in a positive axillary lymph node, prior to the start of NAC. The I-125 seed will be placed simultaneously with the standard I-125 localisation procedure of the breast tumor which precludes extra visits. The I-125 seed will be placed in the lymph node which has been biopsied, i.e. node in which a metastasis was confirmed by pathology.
b) sentinel lymph node biopsy (SLNB): this procedure is a standard dual Tc-99 tracer technique in clinically node negative breast cancer.

Patients who will be participating in this study, will not benefit personally of the RISAS-procedure. However, if RISAS is proven to be an accurate method for the assessment of axillary pCR, future patients will benefit.

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 pathologically confirmed axillary lymph node positive invasive primary breast cancer, treated with neoadjuvant chemotherapy
2. Willing and able to undergo all study procedures
3. Has personally provided written informed consent

Exclusion criteria

1. Age < 18
2. Pregnancy or lactation
3. Contra indication for undergoing SLNB, such as allergic reaction on 99m Technetium or patent blue.
4. Recurrent breast cancer
5. Previous axillary surgery or radiotherapy, (e.g. Hodgkin disease treatment)
6. Patients with periclavicular lymph node metastases (cN3)
7. Patients with advanced breast cancer (i.e. patients with distant metastases, treated without any further surgical procedures)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-03-2017
Enrollment:	248
Type:	Actual

Ethics review

Approved WMO

Date:	24-10-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	22-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

(Rotterdam)

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
ClinicalTrials.gov	NCT02800317
CCMO	NL57700.078.16