ISRCTN11156955 https://doi.org/10.1186/ISRCTN11156955

Optimising the timing and dose of SiennaXP® for sentinel node biopsy in breast cancer: the prospective multicentre SentiDose trial

Submission date
23/01/2018

Recruitment status
No longer recruiting

Registration date
13/02/2018

Overall study status
Completed

Last Edited
01/03/2022

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Breast cancer is the second most common cancer diagnosed in the Swedish population, accounting for more than 8000 new cases and 12% of total cancer cases per year. Breast cancer spreads mainly through the lymphatic system - a system of thin tubes and lymph nodes that carry a clear fluid called lymph around the body. Sentinel lymph nodes (SLNs) are the nodes that first receive lymphatic drainage from the tumour area and these nodes are most likely to harbour metastasizing (spreading) cancer cells when lymphatic metastases occur. Sentinel lymph node biopsy (SLNB) is now the standard technique used in breast cancer patients where the sentinel lymph node is identified, removed, and examined to determine whether cancer cells are present. The gold standard for sentinel node detection is the 'combined technique' which uses both blue dye and a radioisotope injection to locate the sentinel lymph node. The combined technique has drawbacks. The use of radioisotope exposes patients and healthcare workers to radiation, is heavily controlled by legislation (both on the specific training for operators and subsequent disposal of surgical waste), and provides poor pre-operative imaging. Blue dye injection during the operation can obscure the surgical field and frequently leaves a skin residue (tattoo stain), which can take months to fade. There is therefore a need to develop and improve new techniques for detecting sentinel nodes without these drawbacks. The Sienna+® magnetic tracer, which can only be used in combination with the Sentimag® magnetic probe, uses the principle of magnetic detection for sentinel lymph nodes. Clinical studies involving a total of more than 1000 patients have been completed in the past years in hospitals across Europe showing that the magnetic technique is comparable to the gold standard for SLNB, but the injection of 5 ml which is required is thought to cause discomfort to the patient and a brownish discoloration at the injection site. The aim of this study is to investigate the performance of a newer magnetic tracer, SiennaXP®, in lower doses and with a different timing. In particular, 1.5 ml used during the operation and 1.0 ml used 1 to 7 days before surgery are compared to results from previously published studies.

Who can participate?
Patients aged 18 and over with breast cancer who are scheduled for surgery with a SLNB

What does the study involve?
Participants in the group recruited first are treated with an injection of 1.5 ml SiennaXP during the operation. Participants in the group recruited second are treated with 1ml of SiennaXP 1 to 7 days before the operation. To avoid any possible disadvantages of the magnetic technique, participants are also treated with radioisotope and blue dye. During surgery, the surgeon first uses the Sentimag® to find the SLN and then uses the radioisotope probe to confirm. The process is repeated after incision and all SLNs detected are removed and assessed. Patients with staining are followed up for 2 years.

What are the possible benefits and risks of participating?
The new technique might increase the chance of detecting the sentinel node. Possible disadvantages include brown or blue staining of the injection site due to SiennaXP or dye. There is no compensation for taking part in the study.

Where is the study run from?
Uppsala University Hospital (Sweden)

When is the study starting and how long is it expected to run for?
June 2016 to February 2020

Who is funding the study?
Sysmex Europe GmbH

Who is the main contact?
Dr Andreas Karakatsanis

Contact information

Type(s)
Scientific

Contact name
Dr Andreas Karakatsanis

ORCID ID
http://orcid.org/0000-0003-3622-3575

Contact details
Sjukhusvägen, ing 70, Uppsala University Hospital
Uppsala
Sweden
751 85

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
A prospective multicentre study of SiennaXP® in patients with breast cancer undergoing sentinel node biopsy

Study objectives
The detection rate of sentinel node biopsy in patients with early breast cancer with SiennaXP® system at reduced doses and application timepoints of SiennaXP® (1.5 ml in intraoperative application and 1.0 ml applied one to seven days before surgery) is non-inferior to the detection rate of the former tracer Sienna+ and the standard of care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Uppsala Ethics Committee, 05/04/2017, ref: DNR2017/063

Study design
Multicentre non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Sentinel node biopsy in breast cancer

Interventions
The allocation of the cohorts will be performed as follows: The first cohort, i.e. patients with an intraoperative injection of 1.5 ml SiennaXP will be recruited and completed first. The patients recruited thereafter will be included in the second cohort and receive 1ml of SiennaXP 1 to 7 days before the operation. Total duration of follow up is planned for 2 years.

The first patient cohort will receive 1.5 ml SiennaXP® intraoperatively by subareaolar injection into the interstitial tissue. The injection is performed on anaesthetised patients before draping. The seal of the SiennaXP® vial has to be inspected before use to ensure it is unbroken. Do not use if the vial cap is broken, the vial is leaking, or if the expiry date has passed. The amount of 1.5 ml SiennaXP® is drawn via a 5 micron filter needle into a sterile hypodermic syringe of an appropriate volume. The needle and syringe filter are replaced with a fresh sterile injection needle. SiennaXP® is administered by subcutaneous injection into the subareolar interstitial tissue. A vigorous massage at the injection site for at least 5 minutes follows. In the intraoperative setting surgeons need to wait at least 20 minutes before attempting transcutaneous measurement of the axilla. In this time the magnetic tracer migrates through the lymphatic system into the SLNs. Migration time may be prolonged due to high age, obesity and large breast size.

The second patient cohort will receive 1.0 ml SiennaXP® by subareolar or peritumoral injection into the interstitial tissue without massage one to seven days before surgery. The injection is performed on wake patients. The seal of the SiennaXP® vial has to be inspected before use to ensure it is unbroken. Do not use if the vial cap is broken, the vial is leaking, or if the expiry date has passed. The amount of 1.0 ml SiennaXP® is drawn via a 5 micron filter needle into a sterile hypodermic syringe of an appropriate volume. The needle and syringe filter are replaced with a fresh sterile injection needle. SiennaXP® is administered by subcutaneous injection into the subareolar or peritumoral interstitial tissue. No massage is performed.

During surgery, the surgeon will initially use the Sentimag® to localize the SLN and then use the gamma probe to confirm. The process will be repeated after incision and all SLNs detected intra-operatively using the Sentimag®, black staining, gamma probe or blue staining will be excised. After excision each marked lymph node should be measured with the Sentimag® and gamma probe followed by documentation of the values. Afterwards sentinel lymph nodes will be assessed by histology alone and/or by OSNA (One Step Nucleic Acid Amplification). The nodal status is then later related back to the SLN detection rate with the magnetic technique.

Intervention Type
Other

Primary outcome measure
The proportion of successful sentinel node biopsies (SLNB detection rate per patient) with SiennaXP®, measured intraoperatively

Secondary outcome measures
1. The average number of excised sentinel lymph nodes per patient, measured intraoperatively
2. The proportion of SLN detected (nodal detection rate), measured intraoperatively
3. The proportion of pathologically positive results (malignancy rate) per patient and per node, measured intraoperatively
4. All adverse events and serious adverse events, measured intraoperatively
5. All device-related adverse and serious adverse events related to the magnetic detection procedure. Patients will be followed up at baseline (directly postoperatively and at 6, 12, and 24 months postoperatively

Overall study start date
01/06/2016

Completion date

28/02/2020

Eligibility

Key inclusion criteria
1. Subject has a medical record documentation of a diagnosis of primary breast cancer (invasive or in-situ Tis-T2, clinical size up to 5.0 cm)
2. Subject has been scheduled for surgical intervention, with a lymph node biopsy procedure being a part of the surgical plan
3. Subject is ≥18 years old at time of consent
4. Subject has an ECOG performance status of Grade 0-2
5. Subject has a clinical negative node status (N0)
6. Subject has no evidence of general metastases (M0)
7. Subject is available for the follow-up defined in the applied study protocol

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
330

Total final enrolment
328

Key exclusion criteria
1. Subject is pregnant or lactating
2. Subject has evidence of metastatic cancer (M1)
3. Subject has evidence of node positive disease (N1)
4. Subject has locally advanced breast cancer (T4)
5. Subject has previous axilla surgery, reduction mammoplasty, or lymphatic function that is impaired in the surgeon’s judgment
6. Subject has had preoperative radiation therapy to the affected breast or axilla or neoadjuvant chemotherapy.
7. Subject has an iron overload disease
8. Subject has a known hypersensitivity to blue dye
9. Subject has intolerance or hypersensitivity to iron or dextran compounds, or to SiennaXP®
10. Subject has a pacemaker or other implantable device in the chest wall or shoulder
11. Subject is indicated or scheduled for post-operative MRI investigation of the breast
12. Subject has lesions which could pre-operatively only be visualized by MRI investigation of the breast
13. Subject is deprived of liberty or under guardianship

14. Subject is not able to follow and understand the procedures of the study due to mental state or other reasons

Date of first enrolment
01/07/2017

Date of final enrolment
30/12/2018

Locations

Countries of recruitment
Sweden

Study participating centre
Uppsala University Hospital
Uppsala
Sweden
751 85

Sponsor information

Organisation
Uppsala University Hospital (Akademiska)

Sponsor details
-
Uppsala
Sweden
75185

Sponsor type
Hospital/treatment centre

Website
uu.se

ROR
https://ror.org/01apvbh93

Funder(s)

Funder type

Industry

Funder Name
Sysmex Europe GmbH

Results and Publications

Publication and dissemination plan
Study documents will be made available upon request. The study results will be published in an international peer-reviewed journal. Both positive and negative results will be published. Publishing of study results is intended 6 to 12 months after overall trial end date.

Intention to publish date
01/06/2020

Individual participant data (IPD) sharing plan
Patient-level data will be made available at a later date. The data are currently anonymised as hard copies and CRFs are held per study site. Completion of entered data in eCRFs is constantly screened by SAALIG CLINICA, SL,, Milà i Fontanals, 14-26, 1-8, 08012 Barcelona. Study monitoring is performed and co-ordinated by and obligation of KTA Karolinska Trail Alliance, Norra stationsgatan 67, 171 76 Stockholm, Sweden.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		09/02/2021	01/03/2022	Yes	No