ISRCTN36585784 https://doi.org/10.1186/ISRCTN36585784

ATNEC - Axillary management in T1-3N1M0 breast cancer patients with needle biopsy-proven nodal metastases at presentation after neoadjuvant chemotherapy

Submission date
26/10/2020

Recruitment status
Recruiting

Registration date
02/12/2020

Overall study status
Ongoing

Last Edited
16/03/2026

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-further-treatment-to-the-armpit-after-surgery-to-remove-breast-cancer-atnec

Background and study aims
Early-stage breast cancer patients with abnormal-looking armpit lymph glands on an ultrasound scan will have a sample (needle biopsy) of this lymph gland taken. If the sample shows cancer cells are present, patients are often given chemotherapy before surgery (called neoadjuvant chemotherapy) to shrink these cancer cells before their operation. Currently after chemotherapy, all patients undergo breast surgery (lumpectomy or mastectomy) and treatment to their armpit (either removal of all armpit lymph glands or radiotherapy to the armpit). Neoadjuvant chemotherapy results in complete disappearance of cancer in the lymph glands in around 40-70% of patients. For these patients there may be no extra benefit from more treatment to their armpit. Any extra armpit treatment may damage lymphatic drainage from the arm, which could lead to arm swelling (lymphoedema), restricted shoulder movement, pain, numbness and other sensory problems. These side effects make some daily activities difficult for patients, they are distressing and affect their quality of life. They are costly to the NHS in terms of treatments such as physiotherapy and attendance at lymphoedema clinics.
The aim of this study is to find out whether stopping further armpit treatment for patients with no cancer in the lymph glands after chemotherapy is safe, in terms of risk of cancer coming back and fewer lymphoedema cases at 5 years. After neoadjuvant chemotherapy and at the time of breast surgery, patients will undergo removal of at least three lymph glands from the armpit. If there is no cancer in the removed glands, patients will be randomly allocated to receive standard armpit treatment or no further treatment to the armpit.
Results of this study could benefit patients by avoiding unnecessary treatment to the armpit and thus reducing future problems with the arm and shoulder, and possibly improved quality of life and reduced healthcare costs.

Who can participate?
Patients aged 18 or older with early-stage breast cancer that has spread to the lymph gland in their armpit, who will receive (or has received) standard neoadjuvant chemotherapy

What does the study involve?
Eligibility for the randomised portion of the trial will be assessed following completion of neoadjuvant chemotherapy and surgery. The patient's clinician will assess how well their cancer has responded to treatment. If following these assessments, there is no remaining sign of cancer in the patient's armpit lymph glands, then they will be deemed eligible to take part in the randomised stage of the study. Patients eligible for the study will receive either:
1. No further treatment to your armpit, following neoadjuvant chemotherapy and breast surgery, or
2. Further treatment to your armpit, following neoadjuvant chemotherapy and breast surgery
Which treatment patients receive (option 1 or option 2) is decided by a process called randomisation. Neither patients nor their doctor will be able to choose which group is assigned; treatment allocation will be decided randomly by a computer.
If a patient is allocated further treatment to their armpit (option 2), they, together with their doctor, can choose either surgery to remove all remaining lymph glands in the armpit or radiotherapy to the armpit area.
All participants, regardless of which group they are allocated to, will still receive other standard treatment for their breast cancer, such as radiotherapy to the breast and chest wall, and hormone therapy. This treatment will be given as indicated, upon the advice of the clinical team.
Patients who are eligible for the study will also be asked to complete a short questionnaire booklet; there will be five further questionnaire booklets to complete over the course of the study. The researchers will use the responses to assess how patients are feeling with respect to their treatment. Each questionnaire should take approximately 20 minutes to complete.

What are the possible benefits and risks of participating?
The researchers cannot promise that this study will help participants, but it may help patients in the future. Findings from this study will also help inform the future care of patients with early breast cancer that has spread to the armpit. The researchers do not know whether removing further armpit treatment, if there are no signs of cancer left in patients' lymph glands, will have an impact on the risk of their cancer returning – that is why they are doing the study. All participants will be closely monitored by their clinical care team, and if there is any sign of cancer recurrence, their doctor will discuss the best course of action.
X-rays, nuclear medicine imaging and radiotherapy, where appropriate, are part of patients' routine care. If patients take part in this study, they will not undergo any additional imaging or radiotherapy. These procedures use ionising radiation to form images of the body and/or provide treatment and/or provide doctors with other clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. Patients' doctors will discuss other possible side-effects of radiotherapy with them. The chances of these things happening to patients are the same whether they take part in this study or not.
Participants will be asked to complete questionnaires which will take some of their time (about 20 minutes per questionnaire). As the questionnaires form a key part of our data collection for the study, it is important for participants to consider whether they will have the time to complete these fully. Participants will be issued with one questionnaire booklet at trial entry and then five further questionnaires at the following time points: 1 year, 2 years, 3 years, 4 years and 5 years.

Where is the study run from?
University Hospitals of Derby and Burton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2020 to March 2030

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
ATNEC Trial Management team
ATNEC@warwick.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Amit Goyal

ORCID ID
https://orcid.org/0000-0002-2381-8337

Contact details
Chief Investigator
Royal Derby Hospital
Derby
United Kingdom
DE22 3NE
+44 (0)1332 785538
amit.goyal@nhs.net

Type(s)
Public

Contact name
Miss Sophie Nicholls

ORCID ID
https://orcid.org/0000-0003-0371-9777

Contact details
ATNEC Trial Manager
Warwick Clinical Trials Unit
University of Warwick
Coventry
United Kingdom
CV4 7AL
+44 (0)2476524438
ATNEC@warwick.ac.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT04109079

Integrated Research Application System (IRAS)
280105

Central Portfolio Management System (CPMS)
46520

Study information

Scientific Title
ATNEC - Axillary management in T1-3N1M0 breast cancer patients with needle biopsy-proven nodal metastases at presentation after neoadjuvant chemotherapy

Acronym
ATNEC

Study objectives
Omitting further axillary treatment (ALND and ART) for patients with early-stage breast cancer and axillary nodal metastases on needle biopsy, who after NACT have no residual cancer in the lymph nodes on sentinel node biopsy, will be non-inferior to axillary treatment in terms of disease-free survival (DFS) and will result in a reduced risk of lymphoedema at 5 years.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/10/2020, Yorkshire & The Humber – Bradford Leeds Research Ethics Committee (Newcastle Blood Donor Centre, Holland Drive, HRA Newcastle, Newcastle, NE2 4NQ, United Kingdom; +44 (0)207 104 8083, +44 (0)207 104 8088, +44 (0)207 104 8018; bradfordleeds.rec@hra.nhs.uk), ref: 20/YH/0232

Primary study design
Interventional

Study design
Randomized; Both; Design type: Treatment, Process of Care, Surgery, Other, Health Economic

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast cancer

Interventions
Current interventions as of 19/07/2023:

ATNEC is a multi-centre, randomised clinical trial with a non-inferiority endpoint and a pragmatic design. ATNEC will be conducted in patients with early-stage, node-positive breast cancer,

whose usual treatment pathway would be neoadjuvant chemotherapy followed by breast surgery and further treatment to the armpit (lymph node clearance or radiotherapy to the armpit). Patients who have no residual cancer in the lymph glands after chemotherapy will be randomised to either have standard armpit treatment or no further treatment to the armpit.

An integrated feasibility study, with embedded qualitative research, will assess the willingness of clinicians and patients to participate in the ATNEC trial.

Pre-Randomisation:
To be eligible, a patient must be diagnosed with early-stage, confirmed node-positive breast cancer on needle biopsy, and planned to receive chemotherapy first (neoadjuvant chemotherapy) prior to surgery. The patient's primary tumour must have been evaluated for receptor status. Patients can be either female or male, and must be aged 18 years or older.

Patients who are confirmed to be eligible will be invited to take part in the study and if, following review of the patient information sheet, they decide to participate, written informed consent will be obtained.

Once a patient has consented to participate, the site team will be able to register them to the study via the ATNEC online registration portal. The patient will be assigned a unique trial number, which will be used to identify them throughout the study.

It is recommended that the patient's clinical team will mark the abnormal armpit lymph gland – this could be done either by using a clip, carbon dye or by inserting a magnetic seed as per local practice. Patients will then continue to receive neo-adjuvant chemotherapy, as per standard practice.

Following the completion of their chemotherapy, patients will undergo imaging assessment of the lymph glands to check for abnormal-looking lymph glands. If the armpit lymph glands are found to still contain residual cancer cells, the patient will not be eligible for randomisation and will continue with treatment for their cancer, per standard practice. If the ultrasound shows no confirmed evidence of residual cancer, then the patient will proceed to breast surgery (either lumpectomy to remove the lump, or mastectomy to remove the breast). During their operation, a procedure called a sentinel lymph node biopsy will also be performed; this will involve the removal of at least three lymph glands (including the original marked gland). The removed glands will be tested to provide definitive confirmation that the patient has no remaining cancer in their armpit glands. At this point, the patient will be deemed eligible for randomisation.

Patients who are deemed eligible, but have not previously been registered, can also enter the trial at this point. Patients who are willing to participate will be consented after their surgery, registration and randomisation will take place as one process.

Randomisation/Baseline:
Prior to randomisation, patients will be issued with a baseline questionnaire booklet containing the following questionnaires: the lymphoedema and breast cancer questionnaire (LBCQ), a shortened version of the Disability of the Arm, Shoulder and Hand (QuickDASH) questionnaire, a health utilisation questionnaire, and the EQ-5D-5L questionnaire which captures information about a patient's overall health state.

Eligible patients, with continuing consent, will be randomised to the study via the online ATNEC randomisation portal. Patients will be randomised to receive either standard treatment to the armpit (lymph node clearance or radiotherapy to the armpit) or no further armpit treatment.

Follow-Up:
Patients are required to complete five further questionnaire booklets: at 1 year, 2 years, 3 years, 4 years and 5 years post-randomisation. These questionnaire booklets will be posted directly to patients by Warwick Clinical Trials Unit, to complete at home. Posted questionnaires will include a pre-paid return envelope, so completed questionnaires can be returned to the Warwick Clinical Trials Unit.

Beyond the first year, sites will be asked to follow-up patients annually for at least 5 years. Follow-up can be by capturing information from hospital records or by telephone if the treating site has discharged the patient from clinical follow-up. After 5 years, follow-up information will be sought from NHS Digital health records, so long as the patient has given their consent for this.

Radiotherapy Quality Assurance Component:
The ATNEC trial will have an embedded radiotherapy quality assurance programme, coordinated by the National Radiotherapy Quality Assurance (RTTQA) group. Sites will be required to adhere to the specific radiotherapy planning and delivery guidelines, developed by the RTTQA team.

Qualitative Sub-Study:
Qualitative research has been embedded within the recruitment phase to identify and investigate recruitment issues and develop effective and realistic strategies to ensure the success of the trial. Participation in any aspect of the qualitative sub-study is optional.

Patients who appear eligible for ATNEC will be asked for their permission to audio-record their conversations with their doctor up until the point that they make their decision on whether or not to participate. Prior to any commencement of recording, patients will be given a brief patient information sheet explaining the qualitative sub-study. Patients will be given sufficient time to review this and ask any questions. If patients agree to be recorded, they will be asked to sign a consent form, providing permission for the audio-recordings of their consultations.

In addition, patients who were invited to take part in ATNEC (including those who declined to take part) may be invited for interview at a later date to discuss the reasons why they may, or may not, have chosen to take part in the trial. A separate patient information sheet will be provided for this purpose and, should the patient be happy to be interviewed, written informed consent will be obtained. Patients will be asked for their permission to have their interview audio-recorded. This permission is covered in the above-mentioned patient information sheet and informed consent form.

It will be made explicitly clear to patients, at the time of their consultation, or following the informed consent process for the trial, that their participation in the qualitative sub-study is completely optional. The decision of patients who decline to take part will be completely respected, and their medical care will not be affected in any way.

Researchers who are involved in the ATNEC trial consent process (i.e clinicians and research nurses) will also be invited for an interview. Research staff will also be provided with an information sheet and their informed consent will be required prior to any audio-recording of patient consultations and/or interviews.

An overall plan for the qualitative sub-study, including timelines for interviews, is attached to this application.

_____

Previous interventions:

ATNEC is a multi-centre, randomised clinical trial with a non-inferiority endpoint and a pragmatic design. ATNEC will be conducted in patients with early-stage, node-positive breast cancer, whose usual treatment pathway would be neoadjuvant chemotherapy followed by breast surgery and further treatment to the armpit (lymph node clearance or radiotherapy to the armpit). Patients who have no residual cancer in the lymph glands after chemotherapy will be randomised to either have standard armpit treatment or no further treatment to the armpit.

An integrated feasibility study, with embedded qualitative research, will assess the willingness of clinicians and patients to participate in the ATNEC trial.

Pre-Randomisation:
To be eligible, a patient must be diagnosed with early-stage, confirmed node-positive breast cancer on needle biopsy, and planned to receive chemotherapy first (neoadjuvant chemotherapy) prior to surgery. The patient's primary tumour must have been evaluated for receptor status. Patients can be either female or male, and must be aged 18 years or older.

Patients who are confirmed to be eligible will be invited to take part in the study and if, following review of the patient information sheet, they decide to participate, written informed consent will be obtained.

Once a patient has consented to participate, the site team will be able to register them to the study via the ATNEC online registration portal. The patient will be assigned a unique trial number, which will be used to identify them throughout the study.

Prior to receiving treatment, the patient's clinical team will mark the abnormal armpit lymph gland – this could be done either by using a clip, carbon dye or by inserting a magnetic seed as per local practice. Patients will then continue to receive neo-adjuvant chemotherapy, as per standard practice.

Following the completion of their chemotherapy, patients will undergo an ultrasound scan of the lymph glands to check for abnormal-looking lymph glands and if needed needle biopsy. If the armpit lymph glands are found to still contain residual cancer cells, the patient will not be eligible for randomisation and will continue with treatment for their cancer, per standard practice. If the ultrasound shows no confirmed evidence of residual cancer, then the patient will proceed to breast surgery (either lumpectomy to remove the lump, or mastectomy to remove the breast). During their operation, a procedure called a sentinel lymph node biopsy will also be performed; this will involve the removal of at least three lymph glands (including the original marked gland). The removed glands will be tested to provide definitive confirmation that the patient has no remaining cancer in their armpit glands. At this point, the patient will be deemed eligible for randomisation.

Patients who are deemed eligible, but have not previously been registered, can also enter the trial at this point. Patients who are willing to participate will be consented after their surgery, registration and randomisation will take place as one process.

Randomisation/Baseline:
Prior to randomisation, patients will be issued with a baseline questionnaire booklet containing the following questionnaires: the lymphoedema and breast cancer questionnaire (LBCQ), a shortened version of the Disability of the Arm, Shoulder and Hand (QuickDASH) questionnaire, a

health utilisation questionnaire, and the EQ-5D-5L questionnaire which captures information about a patient's overall health state.

Eligible patients, with continuing consent, will be randomised to the study via the online ATNEC randomisation portal. Patients will be randomised to receive either standard treatment to the armpit (lymph node clearance or radiotherapy to the armpit) or no further armpit treatment.

Follow-Up:
Patients are required to complete five further questionnaire booklets: at 1 year, 2 years, 3 years, 4 years and 5 years post-randomisation. These questionnaire booklets will be posted directly to patients by Warwick Clinical Trials Unit, to complete at home. Posted questionnaires will include a pre-paid return envelope, so completed questionnaires can be returned to the Warwick Clinical Trials Unit.

Beyond the first year, sites will be asked to follow-up patients annually for at least 5 years. Follow-up can be by capturing information from hospital records or by telephone if the treating site has discharged the patient from clinical follow-up. After 5 years, follow-up information will be sought from NHS Digital health records, so long as the patient has given their consent for this.

Radiotherapy Quality Assurance Component:
The ATNEC trial will have an embedded radiotherapy quality assurance programme, coordinated by the National Radiotherapy Quality Assurance (RTTQA) group. Sites will be required to adhere to the specific radiotherapy planning and delivery guidelines, developed by the RTTQA team.

Qualitative Sub-Study:
Qualitative research has been embedded within the recruitment phase to identify and investigate recruitment issues and develop effective and realistic strategies to ensure the success of the trial. Participation in any aspect of the qualitative sub-study is optional.

Patients who appear eligible for ATNEC will be asked for their permission to audio-record their conversations with their doctor up until the point that they make their decision on whether or not to participate. Prior to any commencement of recording, patients will be given a brief patient information sheet explaining the qualitative sub-study. Patients will be given sufficient time to review this and ask any questions. If patients agree to be recorded, they will be asked to sign a consent form, providing permission for the audio-recordings of their consultations.

In addition, patients who were invited to take part in ATNEC (including those who declined to take part) may be invited for interview at a later date to discuss the reasons why they may, or may not, have chosen to take part in the trial. A separate patient information sheet will be provided for this purpose and, should the patient be happy to be interviewed, written informed consent will be obtained. Patients will be asked for their permission to have their interview audio-recorded. This permission is covered in the above-mentioned patient information sheet and informed consent form.

It will be made explicitly clear to patients, at the time of their consultation, or following the informed consent process for the trial, that their participation in the qualitative sub-study is completely optional. The decision of patients who decline to take part will be completely respected, and their medical care will not be affected in any way.

Researchers who are involved in the ATNEC trial consent process (i.e clinicians and research nurses) will also be invited for an interview. Research staff will also be provided with an information sheet and their informed consent will be required prior to any audio-recording of patient consultations and/or interviews.

An overall plan for the qualitative sub-study, including timelines for interviews, is attached to this application.

Intervention Type
Mixed

Primary outcome(s)
Co-primary outcomes, collected annually for 5 years:
1. Disease-Free Survival (DFS); defined and calculated as the time from randomisation until the date of the first event of either a loco-regional invasive breast cancer relapse, distant relapse, ipsilateral or contralateral new invasive primary breast cancer or death by any cause or the censor date
2. Lymphoedema: self-reported based on two items from the validated Lymphoedema and Breast Cancer Questionnaire (LBCQ) (arm “swelling now” and arm “heaviness in the past year”). Lymphoedema will be defined as ‘yes’ to both questions at 5 years.

Key secondary outcome(s)
Collected annually for 5 years:
1. Arm function assessed using the shortened version of the Disability of the Arm, Shoulder and Hand (DASH), the 11-item QuickDASH questionnaire, over 5 years
2. Pain intensity and characteristics measured using questions from the Douleur Neuropathique (DN4) and Pain Numeric Rating Scale (NRS) and will relate to the areas affected by surgery and cancer treatment, over 5 years
3. Axillary recurrence-free interval, calculated from the date of randomisation to the date of axillary recurrence or the censor date. Axillary recurrence is defined as pathologically (cytology or biopsy) and/or radiologically confirmed recurrence in lymph nodes draining the primary tumour site. The date of axillary recurrence is the date on which imaging or pathology report (whichever comes first) confirms axillary recurrence. Axillary recurrence will be compared between the two allocated groups over 5 years
4. Overall survival; calculated as the time from randomisation until the date of death by any cause or the censor date. Overall survival will be compared between the two allocated groups over 5 years
5. Local (breast or chest wall) recurrence is defined as pathologically (cytology or biopsy) and/or radiologically confirmed recurrence after mastectomy in the skin or soft tissue of the chest wall within the anatomical area bounded by the mid-sternal line, the clavicle, the posterior axillary line and the costal margin or any type of breast carcinoma in the breast after conservation therapy. The date of local recurrence is the date on which the imaging or pathology report (whichever comes first) confirms local recurrence. Local recurrence will be compared between the two allocated groups over 5 years
6. Regional (nodal) recurrence is defined as pathologically (cytology or biopsy) and/or radiologically confirmed recurrent tumour in the lymph nodes in the ipsilateral axilla, infraclavicular, supraclavicular fossa, interpectoral area or ipsilateral internal mammary chain. The date of regional recurrence is the date on which the imaging or pathology report (whichever comes first) confirms local recurrence. Regional (nodal) recurrence will be compared between the two allocated groups over 5 years
7. Distant metastasis is defined as confirmed metastasis (positive pathology and/or definitive

evidence on imaging) in all other sites of recurrence and may include those classified as: soft-tissue category, visceral category, central nervous system and skeletal spread. The date of distant metastasis is the date on which the imaging or pathology report (whichever comes first) confirms metastasis. Distant metastases will be compared between the two allocated groups over 5 years.
8. Contralateral breast cancer is defined as a new primary malignancy in the opposite breast unless obviously contiguous with recurrent chest wall disease or proven on cytology/biopsy to be of metastatic origin. Contralateral breast cancers will be compared between the two allocated groups over 5 years.
9. Non-breast cancer is defined as any new non-breast primary malignancy, except for basal or squamous cell cancer of the skin, in situ carcinoma of the cervix, or in situ or stage 1 melanoma. New breast cancers will be compared between the two allocated groups over 5 years.
10. Economic evaluation (data to be collected annually, over 5 years, through annual follow-up and patient questionnaires):
10.1. Costs to the NHS and participants will be compared between the two allocated groups over 5 years
10.2. Quality-adjusted life years (QALYs) will be compared between the two groups over 5 years. QALYs based on responses to the EQ-5D-5L administered at baseline, 12, 24, 36, 48, and 60 months post-randomisation
10.3. Incremental cost per disease-free interval over 5 years
10.4. Incremental cost per lymphoedema avoided over 5 years
10.5. Incremental cost per QALY gained over 5 years
10.6. Incremental cost per QALY over the estimated lifetime of a participant with early-stage breast cancer

Completion date
01/03/2030

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 16/03/2026:

1. Age ≥ 18 years
2. Male or female
3. cT1-3N1M0 breast cancer at diagnosis (prior to NACT) as per AJCC 8th edition
3.1. Patients with occult primary invasive breast cancer (no identifiable invasive cancer in the breast) with FNA or core biopsy proven nodal metastases are eligible for the study.
4. FNA or core biopsy confirmed axillary nodal metastases at presentation
5. Oestrogen receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Imaging of the axilla, as required, to assess response to NACT (per local guidelines)
8. Undergo a dual tracer sentinel node biopsy (SNB) after NACT with at least 3 nodes removed.
8.1. If a single tracer SNB is performed: the patient is eligible only if the involved node is marked before or during NACT, and at least 3 nodes (including the marked node) are removed during sentinel node biopsy.
8.2. If the node is not marked or the marked node is not removed: the patient is eligible only if the histology report shows evidence of down-staging with complete pathological response e.g., fibrosis or scarring in at least one node and at least 3 nodes removed.
8.3. If fewer than 3 nodes are found on histology: the patient is eligible only if BOTH points a)

and b), below, are met:
a) involved node was marked and removed during SNB; and
b) removed marked node shows evidence of downstaging on histology e.g. fibrosis or scarring.
9. If the sentinel node(s) cannot be localised on SNB: axillary node sampling should be performed, the patient will be eligible if at least 3 nodes are removed.
10. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macro metastasis)
11. Patients with complete pathological response in the axilla but residual disease in the breast post NACT are eligible for the study
12. Patients who are cN0 (node negative) at initial presentation, with a negative sentinel node post NACT showing evidence of treatment response or downstaging will be eligible, provided at least 3 nodes are removed.

_____

Previous inclusion criteria as of 05/02/2024:

1. Age ≥18 years
2. Male or female
3. cT1-3N1M0 breast cancer at diagnosis (prior to NACT) as per AJCC 8th edition
3.2 Patients with occult primary invasive breast cancer (no identifiable invasive cancer in the breast) with FNA or core biopsy provide nodal metastases are also eligible for the study.
4. FNA or core biopsy confirmed axillary nodal metastases at presentation
5. Oestrogen receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Imaging of the axilla, as required, to assess response to NACT (per local guidelines)
8. Undergo a dual tracer sentinel node biopsy (SNB) after NACT with at least 3 nodes removed in total (sentinel nodes and marked node).
8.1 If a single tracer SNB is performed: the patient is eligible only if the involved node is marked before or during NACT, and at least 3 nodes (including the marked node) are removed during sentinel node biopsy.
8.2 If the node is not marked, or marked node is not removed: the patient is eligible only if the histology report shows evidence of downstaging with complete pathological response e.g. fibrosis or scarring in at least one node and at least 3 nodes removed.
8.3 If fewer than 3 nodes are found on histology: the patient is eligible only if BOTH points a) and b), below, are met:
a) involved node was marked and removed during SNB; and
b) removed marked node shows evidence of downstaging on histology e.g. fibrosis or scarring.
8.4 If the sentinel node(s) cannot be localised on SNB: axillary node sampling should be performed, the patient will be eligible if at least 3 nodes are removed (including the marked node).
9. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macrometastasis)

_____

Previous inclusion criteria as of 19/07/2023 to 05/02/2024:

1. Age ≥18 years
2. Male or female
3. cT1-3N1M0 breast cancer at diagnosis (prior to NACT) as per AJCC 8th edition
4. FNA or core biopsy confirmed axillary nodal metastases at presentation

5. Oestrogen receptor, progesterone receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Imaging of the axilla to assess response to NACT (as per local guidelines)
8. Undergo dual tracer sentinel node biopsy after NACT and at least 3 nodes removed (sentinel nodes and marked node).
8.1 If a single tracer is used, the patient will be eligible if the involved node is marked before or during NACT, and the marked node and at least 3 nodes (including the marked node) are removed during sentinel node biopsy.
8.2 If axillary node sampling is performed following failed localisation of sentinel nodes, patient will be eligible if at least three nodes removed (including the marked node).
8.3 If node is not marked, or marked node is not removed, the patient will be eligible if the histology report shows evidence of downstaging with complete pathological response e.g. fibrosis or scarring in at least one node and at least 3 nodes removed.
8.4 If fewer than 3 nodes are found on histology, the patient is eligible if: a) involved node was marked and removed during SNB; and b) removed marked node shows evidence of downstaging on histology e.g. fibrosis or scarring.
9. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macrometastasis)

———

Previous inclusion criteria:

1. Age ≥18 years
2. Male or female
3. T1-3N1M0 breast cancer at diagnosis (prior to NACT)
4. FNA or core biopsy confirmed axillary nodal metastases at presentation
5. Oestrogen receptor, progesterone receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Ultrasound of the axilla at completion of NACT
8. Undergo dual tracer sentinel node biopsy after NACT and at least 3 nodes removed (sentinel nodes and marked node). If axillary node sampling is performed following failed localisation of sentinel nodes, patient will be eligible if at least three nodes removed (including the marked node)
9. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macrometastasis)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 16/03/2026:

1. Bilateral synchronous invasive breast cancer
2. Sentinel node biopsy prior to NACT
3. Previous axillary nodal surgery on the same body side as the scheduled targeted sampling
4. Any previous cancer within last 5 years or concomitant malignancy except
4.1. basal or squamous cell carcinoma of the skin
4.2. in situ carcinoma of the cervix
4.3. in situ or stage 1 melanoma
4.4. contra- or ipsilateral in situ breast cancer
4.5. chronic lymphocytic leukaemia not on treatment

_____

Previous exclusion criteria as of 19/07/2023:

1. Bilateral synchronous invasive breast cancer
2. Sentinel node biopsy prior to NACT
3. Previous axillary surgery on the same body side as the scheduled targeted sampling
4. Any previous cancer within 5 years or concomitant malignancy except:
4.1. Basal or squamous cell carcinoma of the skin
4.2. In situ carcinoma of the cervix
4.3. In situ melanoma
4.4. Contra- or ipsilateral in situ breast cancer

_____

Previous exclusion criteria:

1. Bilateral invasive breast cancer
2. Sentinel node biopsy prior to NACT
3. Marked node not removed except where the node/s removed show evidence of down-staging with complete pathological response e.g. fibrosis or scarring
4. Previous axillary surgery on the same body side as the scheduled targeted sampling
5. Any previous cancer within 5 years or concomitant malignancy except:
5.1. Basal or squamous cell carcinoma of the skin
5.2. In situ carcinoma of the cervix
5.3. In situ melanoma
5.4. Contra- or ipsilateral in situ breast cancer

Date of first enrolment
21/12/2020

Date of final enrolment

28/02/2030

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Isle of Man

Study participating centre
NHS Grampian
Summerfield House
2 Eday Road
ABERDEEN
Scotland
AB15 6RE

Study participating centre
CAMBRIDGE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
ADDENBROOKES HOSPITAL
HILLS ROAD
CAMBRIDGE
England
CB2 0QQ

Study participating centre
FRIMLEY HEALTH NHS FOUNDATION TRUST
PORTSMOUTH ROAD
FRIMLEY
CAMBERLEY
England
GU16 7UJ

Study participating centre

NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
Scotland
G12 0XH

Study participating centre
NHS Forth Valley
33 Spittal Street
Stirling
Scotland
FK8 1DX

Study participating centre
NHS Ayrshire and Arran
PO Box 13, Boswell House
10 Arthur Street
AYR
Scotland
KA7 1QJ

Study participating centre
Belfast Health & Social Care Trust
Trust Headquarters
A Floor - Belfast City Hospital
Lisburn Road
Belfast
Northern Ireland
BT9 7AB

Study participating centre
NHS Borders
Newstead
MELROSE
Scotland
TD6 9DB

Study participating centre

NORTH BRISTOL NHS TRUST
SOUTHMEAD HOSPITAL
SOUTHMEAD ROAD
WESTBURY-ON-TRYM
BRISTOL
England
BS10 5NB

Study participating centre
CHELSEA AND WESTMINSTER HOSPITAL NHS FOUNDATION TRUST
CHELSEA & WESTMINSTER HOSPITAL
369 FULHAM ROAD
LONDON
England
SW10 9NH

Study participating centre
WYE VALLEY NHS TRUST
COUNTY HOSPITAL
UNION WALK
HEREFORD
England
HR1 2ER

Study participating centre
OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
JOHN RADCLIFFE HOSPITAL
HEADLEY WAY
HEADINGTON
OXFORD
England
OX3 9DU

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
England
L7 8XP

Study participating centre
ST HELENS AND KNOWSLEY TEACHING HOSPITALS NHS TRUST
WHISTON HOSPITAL
WARRINGTON ROAD
PRESCOT
England
L35 5DR

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
PLYMOUTH
England
PL6 8DH

Study participating centre
THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
FREEMAN HOSPITAL
FREEMAN ROAD
HIGH HEATON
NEWCASTLE-UPON-TYNE
England
NE7 7DN

Study participating centre
NORTH TEES AND HARTLEPOOL NHS FOUNDATION TRUST
UNIVERSITY HOSPITAL OF HARTLEPOOL
HOLDFORTH ROAD
HARTLEPOOL
CLEVELAND
England
TS24 9AH

Study participating centre
UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST
LEICESTER ROYAL INFIRMARY
INFIRMARY SQUARE
LEICESTER
England
LE1 5WW

Study participating centre
UNITED LINCOLNSHIRE HOSPITALS NHS TRUST
LINCOLN COUNTY HOSPITAL
GREETWELL ROAD
LINCOLN
England
LN2 5QY

Study participating centre
WEST HERTFORDSHIRE HOSPITALS NHS TRUST
TRUST OFFICES
WATFORD GENERAL HOSPITAL
VICARAGE ROAD
WATFORD
England
WD18 0HB

Study participating centre
Somerset NHS Foundation Trust
Trust Management
Lydeard House
Musgrove Park Hospital
Taunton
England
TA1 5DA

Study participating centre
NHS Highland
Reay House
17 Old Edinburgh Road
INVERNESS
Scotland
IV2 3HG

Study participating centre
ROYAL CORNWALL HOSPITALS NHS TRUST
ROYAL CORNWALL HOSPITAL
TRELISKE
TRURO
England
TR1 3LJ

Study participating centre
UNIVERSITY HOSPITALS OF DERBY AND BURTON NHS FOUNDATION TRUST
ROYAL DERBY HOSPITAL
UTTOXETER ROAD
DERBY
England
DE22 3NE

Study participating centre
ROYAL FREE LONDON NHS FOUNDATION TRUST
ROYAL FREE HOSPITAL
POND STREET
LONDON
England
NW3 2QG

Study participating centre
Mid and South Essex NHS Foundation Trust
Prittlewell Chase
Westcliff-on-sea
England
SS0 0RY

Study participating centre
UNIVERSITY HOSPITALS OF MORECAMBE BAY NHS FOUNDATION TRUST
WESTMORLAND GENERAL HOSPITAL
BURTON ROAD
KENDAL
England
LA9 7RG

Study participating centre
UNIVERSITY HOSPITALS OF NORTH MIDLANDS NHS TRUST
NEWCASTLE ROAD
STOKE-ON-TRENT
England
ST4 6QG

Study participating centre

BRIGHTON AND SUSSEX UNIVERSITY HOSPITALS NHS TRUST
ROYAL SUSSEX COUNTY HOSPITAL
EASTERN ROAD
BRIGHTON
England
BN2 5BE

Study participating centre
Hywel Dda NHS Trust
Hafan Derwen
Jobs Well Road
Carmarthen
Wales
SA31 3BB

Study participating centre
ASHFORD AND ST PETER'S HOSPITALS NHS FOUNDATION TRUST
ST PETERS HOSPITAL
GUILDFORD ROAD
CHERTSEY
England
KT16 0PZ

Study participating centre
Airedale NHS Foundation Trust
Airedale General Hospital
Skipton Road
Steeton
Keighley
England
BD20 6TD

Study participating centre
MID YORKSHIRE HOSPITALS NHS TRUST
PINDERFIELDS HOSPITAL
ABERFORD ROAD
WAKEFIELD
England
WF1 4DG

Study participating centre

CALDERDALE AND HUDDERSFIELD NHS FOUNDATION TRUST
ROYAL INFIRMARY
ACRE STREET
HUDDERSFIELD
England
HD3 3EA

Study participating centre
WRIGHTINGTON, WIGAN AND LEIGH NHS FOUNDATION TRUST
THE ELMS
ROYAL ALBERT EDWARD INFIRMARY
WIGAN LANE
WIGAN
England
WN1 2NN

Study participating centre
BOLTON NHS FOUNDATION TRUST
THE ROYAL BOLTON HOSPITAL
MINERVA ROAD
FARNWORTH
BOLTON
England
BL4 0JR

Study participating centre
EAST CHESHIRE NHS TRUST
MACCLESFIELD
DISTRICT GEN HOSPITAL
VICTORIA ROAD
MACCLESFIELD
England
SK10 3BL

Study participating centre
MANCHESTER UNIVERSITY NHS FOUNDATION TRUST
COBBETT HOUSE
OXFORD ROAD
MANCHESTER
England
M13 9WL

Study participating centre
SOUTH TEES HOSPITALS NHS FOUNDATION TRUST
JAMES COOK UNIVERSITY HOSPITAL
MARTON ROAD
MIDDLESBROUGH
CLEVELAND
England
TS4 3BW

Study participating centre
UNIVERSITY COLLEGE LONDON HOSPITALS NHS FOUNDATION TRUST
250 EUSTON ROAD
LONDON
England
NW1 2PG

Study participating centre
NHS Lanarkshire
14 Beckford Street
HAMILTON
Scotland
ML3 0TA

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
Scotland
EH1 3EG

Study participating centre
THE ROTHERHAM NHS FOUNDATION TRUST
MOORGATE ROAD
ROTHERHAM
England
S60 2UD

Study participating centre

DONCASTER AND BASSETLAW TEACHING HOSPITALS NHS FOUNDATION TRUST
DONCASTER ROYAL INFIRMARY
ARMTHORPE ROAD
DONCASTER
England
DN2 5LT

Study participating centre
SHEFFIELD TEACHING HOSPITALS NHS FOUNDATION TRUST
NORTHERN GENERAL HOSPITAL
HERRIES ROAD
SHEFFIELD
England
S5 7AU

Study participating centre
ROYAL BERKSHIRE NHS FOUNDATION TRUST
ROYAL BERKSHIRE HOSPITAL
LONDON ROAD
READING
England
RG1 5AN

Study participating centre
UNIVERSITY HOSPITALS BIRMINGHAM NHS FOUNDATION TRUST
QUEEN ELIZABETH HOSPITAL
MINDELSOHN WAY
EDGBASTON
BIRMINGHAM
England
B15 2GW

Study participating centre
LUTON AND DUNSTABLE UNIVERSITY HOSPITAL NHS FOUNDATION TRUST
LEWSEY ROAD
LUTON
England
LU4 0DZ

Study participating centre

ROYAL DEVON AND EXETER NHS FOUNDATION TRUST
ROYAL DEVON & EXETER
HOSPITAL
BARRACK ROAD
EXETER
England
EX2 5DW

Study participating centre
SANDWELL AND WEST BIRMINGHAM HOSPITALS NHS TRUST
CITY HOSPITAL
DUDLEY ROAD
BIRMINGHAM
England
B18 7QH

Study participating centre
THE ROYAL MARSDEN NHS FOUNDATION TRUST
FULHAM ROAD
LONDON
England
SW3 6JJ

Study participating centre
NORTH MIDDLESEX UNIVERSITY HOSPITAL NHS TRUST
NORTH MIDDLESEX HOSPITAL
STERLING WAY
LONDON
England
N18 1QX

Study participating centre
NORTH CUMBRIA INTEGRATED CARE NHS FOUNDATION TRUST
VOREDA HOUSE
PORTLAND PLACE
PENRITH
England
CA11 7BF

Study participating centre

East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Haslingden Road
Blackburn
England
BB2 3HH

Study participating centre
Hull University Teaching Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
Hull
England
HU3 2JZ

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
England
W2 1BL

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Hospital
Arrowe Park Road
Upton
Wirral
England
CH49 5PE

Study participating centre
Countess of Chester Hospital NHS Foundation Trust
Countess of Chester Health Park
Liverpool Road
Chester
England
CH2 1UL

Study participating centre
County Durham and Darlington NHS Foundation Trust
Darlington Memorial Hospital
Hollyhurst Road
Darlington
England
DL3 6HX

Study participating centre
NHS Dumfries and Galloway
Grierson House
The Crichton
Bankend Road
Dumfries
Scotland
DG1 4ZG

Study participating centre
James Paget University Hospitals NHS Foundation Trust
Lowestoft Road
Gorleston
Great Yarmouth
England
NR31 6LA

Study participating centre
King's College Hospital NHS Foundation Trust
King's College Hospital
Denmark Hill
London
England
SE5 9RS

Study participating centre
Mid Cheshire Hospitals NHS Foundation Trust
Leighton Hospital
Leighton
Crewe
England
CW1 4QJ

Study participating centre
Milton Keynes University Hospital NHS Foundation Trust
Standing Way
Eaglestone
Milton Keynes
England
MK6 5LD

Study participating centre
The Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
England
WV10 0QP

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
England
NE9 6SX

Study participating centre
NHS Fife
Hayfield House
Hayfield Road
Kirkcaldy
Scotland
KY2 5AH

Study participating centre
The Shrewsbury and Telford Hospital NHS Trust
Mytton Oak Road
Shrewsbury
England
SY3 8XQ

Study participating centre

Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
Duckworth Lane
Bradford
England
BD9 6RJ

Study participating centre
Tameside and Glossop Integrated Care NHS Foundation Trust
Tameside General Hospital
Fountain Street
Ashton-under-lyne
England
OL6 9RW

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Hospital
Clatterbridge Road
Bebington
Wirral
England
CH63 4JY

Study participating centre
Buckinghamshire Healthcare NHS Trust
Amersham Hospital
Whielden Street
Amersham
England
HP7 0JD

Study participating centre

York and Scarborough Teaching Hospitals NHS Foundation Trust
York Hospital
Wigginton Road
York
England
YO31 8HE

Study participating centre
Victoria Hospital (blackpool)
Whinney Heys Road
Blackpool
England
FY3 8NR

Study participating centre
Croydon University Hospital
London Road
Croydon
England
CR7 7YE

Study participating centre
Lister Hospital
Coreys Mill Lane
Stevenage
England
SG1 4AB

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
England
IP4 5PD

Study participating centre
King Edward VII Hospital (Parapet)
St. Leonards Road
Windsor
England
SL4 3DP

Study participating centre
University Hospital Galway
Newcastle Road
Galway NO COUNTRY SPECIFIED, assuming England
England
H91 YR71

Study participating centre
Cheltenham General Hospital
Sandford Road
Cheltenham
England
GL53 7AN

Study participating centre
Harrogate District Hospital
Lancaster Park Road
Harrogate
England
HG2 7SX

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
England
PR2 9HT

Study participating centre
North Tyneside General Hospital
Rake Lane
North Shields
England
NE29 8NH

Study participating centre

Queen Alexandra Hospital
Southwick Hill Road
Cosham
Portsmouth
England
PO6 3LY

Study participating centre
East Surrey Hospital
Canada Avenue
Redhill
England
RH1 5RH

Study participating centre
Singleton Hospital
Sketty Lane
Sketty
Swansea
Wales
SA2 8QA

Study participating centre
Russells Hall Hospital
Pensnett Road
Dudley
England
DY1 2HQ

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
England
WV10 0QP

Study participating centre
Whittington Hospital
Magdala Avenue
London

England
N19 5NF

Study participating centre
Worcestershire Royal Hospital
Charles Hastings Way
Worcester
England
WR5 1DD

Study participating centre
Yeovil District Hospital
Higher Kingston
Yeovil
England
BA21 4AT

Sponsor information

Organisation
University Hospitals of Derby and Burton NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research; Grant Codes: NIHR128311

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request. Participant data is stored on a secure server at WCTU where each participant has been assigned a de-identified trial number. Any requests for access to the trial data should be sent to the CI who will inform the data custodians and agreement will be made through the data access committee which will comprise of the principal investigators from the trial management group. For each data sharing request, it is essential that a proforma is completed which will describe the purpose, scope, data items requested, analysis plan and acknowledgment of the trial management team. Requestors who are granted access to the data will be required to complete a data-sharing agreement which will be signed by the requester, sponsor and principal investigator(s). The researchers anticipate that data sharing will be possible after the publication of the primary endpoint of the trial.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes