ISRCTN17170034 https://doi.org/10.1186/ISRCTN17170034

Can patients with residual cancer after chemotherapy for early breast cancer be identified with multiple ultrasound-guided biopsies?

Submission date 10/12/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 21/01/2019	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 19/12/2024	**Condition category** Cancer	[_] 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-study-looking-at-ultrasound-guided-biopsies-for-breast-cancer-nostra

Study website
https://www.birmingham.ac.uk/research/crctu/trials/nostra-feas/index.aspx

Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
2016-004583-19

IRAS number
211232

ClinicalTrials.gov number
NCT04118192

Secondary identifying numbers
CPMS 38071, IRAS 211232

Study information

Scientific Title
A prospective non-randomised multi-centre feasibility study to assess if patients with residual cancer following dual-targeted neoadjuvant chemotherapy treatment for HER2-positive, ER-negative early breast cancer can be identified by multiple ultrasound-guided tumour bed core biopsies

Acronym
NOSTRA-Feasibility Study

Study objectives
The NOSTRA-Feasibility study is designed to determine if it is safe to omit surgery after the planned neoadjuvant chemotherapy plus dual-targeted anti-HER2 treatment. The study is needed to determine whether patients with residual cancer can be identified by histological examination of multiple ultrasound-guided tumour bed core biopsies following dual-targeted neoadjuvant treatment for HER2-positive, ER-negative early primary breast cancer and whether there is concordance between local pathology reporting and central pathology reporting by the trials expert pathologists.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/11/2018, West Midlands- Solihull Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)207 104 8191, (0)207 104 8269; solihull.rec@hra.nhs.uk), ref. 18/WM/0257

Study design
Non-randomised; Observational; Design type: Validation of investigation /therapeutic procedures

Primary study design
Observational

Secondary study design

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

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

Interventions
Current interventions as of 19/12/2024:

STUDY DESIGN:
The NOSTRA-Feasibility study is a prospective non-randomised, single-arm, multicentre, feasibility study for a proposed future phase III clinical trial. The recruitment target for this feasibility study is 150 patients over 18 months. It is anticipated that up to 30 sites in the UK will be opened to recruitment. The treatment period is anticipated to be 12 months followed by follow-up at 12 months.

There are multiple aspects to this study and these are broken down in the sections below:

COLLECTION OF TUMOUR BED BIOPSIES:
Following neoadjuvant treatment, all patients will undergo multiple US-guided tumour bed core biopsies prior to surgery. Most patients will have 8 cores taken but it is recognised that in patients with small tumours, or if technical or patient issues dictate, not all 8 cores will be possible.

A fan of paired cores will be taken, working from the central (nipple) tumour margin across the tumour to the peripheral edge of the original tumour bed, as described below:
1. Two cores from the medial peripheral margin
2. Two cores from the central tumour bed medial to marker clip
3. Two cores from the central tumour bed lateral to marker clip
4. Two cores from the lateral peripheral margin

SURGERY:
All patients will proceed to surgery in the NOSTRA-Feasibility Study. Surgery should proceed when the Investigator is satisfied that the patient is sufficiently recovered from neoadjuvant chemotherapy, at the earliest 3 weeks after day 1 of the last cycle of chemotherapy, and ideally within 6 weeks of day 1 of the last cycle of chemotherapy. Surgery to the breast will be according to local protocol and finally determined after post-neoadjuvant Multidisciplinary Team meetings where all imaging and clinical factors will be reviewed. Appropriate surgical options will be discussed and agreed with patients as standard clinical practice.

CENTRAL HISTOPATHOLOGY REVIEW:
All material from the diagnostic core biopsies, surgical excision specimens (including axilla biopsy specimens and SLNB specimens) and protocol defined tumour bed core biopsies will be handled and reported in local laboratories as per UK NHS Breast Screening Programme and Royal College of Pathologists joint guidelines. Local pathologists will ensure that accurate

documentation of block taking is included in the histology reports from the surgically excised lesions (as per UK guidelines) in order to allow the central review to re-assess and, for example, to determine tumour size in more than one dimension. All material will be sent to HBRC for storage prior to central histopathology review.

There will be a central histopathology review of all patients to determine pCR and RCB. The NOSTRA-Feasibility Study pathologists will review all material from the diagnostic core biopsies, surgical excision specimens (including axilla biopsy specimens and Sentinel Lymph Node Biopsy (SLNB) specimens) and protocol defined tumour bed core biopsies. The central review pathologists will record the RCB score and group, as this is not routine practice in the UK. pCR is defined on the basis of central histopathology review of the surgical slides.

TRANSLATIONAL RESEARCH:
Tissue samples from this study will be an invaluable research resource for future studies. Patients are asked to consent for any tissue remaining at the end of the study to be stored for use in other ethically approved research projects. Patients are asked to gift tumour samples stored in any NHS Trust that are surplus to clinical requirements to the study.

Upon completion of central histopathology review, the primary diagnostic core biopsies, surgical excision specimens (including axilla biopsy specimens and Sentinel Lymph Node Biopsy (SLNB) specimens) and protocol defined tumour bed core biopsies will be kept at the HBRC for research purposes.

BLOOD COLLECTION FOR ctDNA SUB-STUDY (OPTIONAL):
Patients willing to provide blood samples will be asked to provide informed consent to take part in the optional ctDNA substudy. If a patient is unwilling to take part in this aspect of the study, they are still permitted to enter the study.

For patient's that have provided consent for the collection of blood samples, a blood sample should be obtained at three timepoints:
1. Prior to commencing neoadjuvant treatment (pre-cycle 1 of chemotherapy and dua-targeted anti-HER2 treatment)
2. Post-cycle 1 of neoadjuvant treatment
3. After surgery is complete (first visit to clinic post-surgery)

These timepoints should coincide with routine blood tests taken within clinic. Up to 70 ml of blood will be taken (9 ml in EDTA tube and 60 ml in ctDNA tubes). Sites are not required to process the blood samples. The blood samples should be packaged and shipped together with the Blood Sample Collection Form on the same day to the Institute of Cancer and Genomic Sciences, University of Birmingham.

PATIENT PATHWAY TO STUDY ENTRY:
Potential patients will be identified at the Multidisciplinary Team meeting in participating NHS hospitals. Tests performed to assess eligibility will be identical to those performed as part of standard care in the vast majority of hospitals (sites). Patients meeting the criteria for study entry will be given a Patient Information Sheet and if willing to participate will be asked to sign and date an Informed Consent Form.

Screening Visit:
As part of the screening process and to confirm eligibility, the following procedures will be undertaken as part of standard routine practice:
1. Diagnostic biopsy and ultrasound visible marker clip insertion

2. Medical history
3. Full physical examination including height and weight
4. Molecular biomarker (ER, PgR and HER2) status
5. Radiological measurement of primary breast tumour(s) by standard practice ultrasound and mammogram
6. Clinical tumour measurements (caliper)
7. Fine Needle Aspirate (FNA) or core biopsy of clinically or radiologically enlarged/abnormal axillary nodes is required to define involvement
8. TNM staging to exclude metastatic disease in accordance with standard early breast cancer practice according to local site policy
9. Left Ventricular Ejection Fraction (LVEF) measured by Echocardiogram (ECHO) or Multi gated Acquisition (MUGA) within 12 weeks prior to study entry
10. Eastern Co-operative Oncology Group (ECOG) performance status
11. Sentinel lymph node biopsy at clinician's discretion and only if no abnormal lymph nodes detected on ultrasound
12. Biochemical screen (ALT or AST, ALP, Bilirubin, Urea, Creatinine, Sodium, Potassium, Estimated Glomerular Filtration Rate)
13. Pregnancy test for females of child-bearing potential
14. Routine full blood count to include haemoglobin, white blood cell count including differential count and platlets.

Patients with abnormal blood test results would be considered ineligible for the study. Investigators will be expected to maintain details of all patients screened for the NOSTRA-Feasibility Study on the Patient Screening/Enrolment Log.

Study Entry:
Patients will be registered into the study once eligibility is confirmed through screening assessments and patient has given written informed consent. Patient registration will be performed electronically via the electronic Remote Data Capture (eRDC) system developed by CRCTU. The Investigator must provide name of site and responsible Investigator, patient's initials, date of birth, patient's hospital number, date of informed consent and the intended treatment regimen option at the discretion of the treating clinician at registration. At the end of the registration process patients will be assigned a unique patient trial number.

All patients will receive neoadjuvant chemotherapy plus dual-targeted anti-HER2 treatment with trastuzumab and pertuzumab using approved combination regimes with established efficacy and tolerability at the discretion of the treating clinician. The three NICE approved treatment regimens are:

REGIMEN 1: 5-Fluorouracil 500mg/m2*, Epirubicin 100mg/m2, Cyclophosphamide 600mg/m2, cycle 1-3 with Pertuzumab 840mg cycle 1 and 420mg cycles 2 and 3 and Trastuzumab 8mg/kg cycle 1 and 6mg/kg cycle 2 and 3, three weekly (3 cycles)
Followed by Docetaxel with Pertuzumab and Trastuzumab:
Docetaxel 75mg/m2 cycle 4 escalating to 100mg/m2 in the absence of dose limiting toxicity for cycle 5 and 6 with Pertuzumab 420mg cycle 4-6 and Trastuzumab 6mg/kg cycles 4-6, three weekly (3 cycles)

REGIMEN 2: 5-Fluorouracil 500mg/m2*, Epirubicin 100mg/m2, Cyclophosphamide 600mg/m2, three weekly (3 cycles)
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Docetaxel 75mg/m2 cycle 4 escalating to 100mg/m2 in the absence of dose limiting toxicity for cycle 5 and 6 with Pertuzumab 840mg cycle 4 and 420mg cycles 5 and 6 and Trastuzumab 8mg /kg cycle 4 and 6mg/kg cycles 5 and 6, three weekly (3 cycles)

REGIMEN 3: Docetaxel 75mg/m2 and Carboplatin AUC 6 with Pertuzumab 840mg cycle 1 and 420mg cycles 2-6 and Trastuzumab 8mg/kg cycle 1 and 6mg/kg cycles 2-6,three weekly (6 cycles)
*Omission of 5-Fluorouracil at the discretion of the treating Investigator
However, if a site wishes to use a different regimen, it must be approved by the Trial Management Group (TMG) before site activation. (added 07/02/2022)
If a site subsequently wishes to change their chosen regimen(s), then this must be approved before patient registration. (added 07/02/2022)

Adjuvant Treatment: Traztuzumab must be continued following completion of neoadjuvant chemotherapy regimen. All patients will continue with adjuvant trastuzumab to receive a total of 18 cycles, +/- radiotherapy

On completion of the registration process, an email to key personnel (including the Investigator, the person performing the registration and responsible pharmacist) will be sent via eRDC confirming patient's entry into the study.
Ideally patients should be entered into the study as soon as possible and within a maximum of 9 weeks (unless by patient choice) from the initial core biopsy result. Chemotherapy should ideally start within two weeks of registration.

On-treatment assessments:
Prior to 1st cycle of neoadjuvant chemotherapy and anti-HER2 treatment: If the patient has provided consent to take part in the ctDNA substudy, a blood sample will be taken prior to commencing the first cycle of neoadjuvant treatment. This will be taken in conjunction with the routine blood samples.

Prior to each cycle of neoadjuvant chemotherapy and anti-HER2 treatment: The following assessments will be performed prior to day 1 of each cycle of neoadjuvant chemotherapy (excluding cycle 1) and are envisaged to be part of standard practice:
1. Vital signs (blood pressure, pulse, temperature)
2. Full blood count within 3 days prior to day 1 of each 3 weekly treatment cycle to include haemoglobin, white blood cell count including differential count and platelets
3. Biochemical screen within 3 days prior to treatment cycle to include ALT or AST, ALP, Bilirubin, Urea, Creatinine, Sodium and Potassium
4. Review of adverse events. CTCAE version 4.0 will be used to grade adverse events.
5. Clinical tumour measurement (calipers): This is not required unless there is a concern or at discretion of the Investigator

End of Cycle 3 of neoadjuvant chemotherapy and anti-HER2 treatment: A clinical tumour assessment by caliper is mandatory to confirm absence of early disease progression at the end of cycle 3 (i.e. prior to commencing cycle 4 treatment). LVEF will also be measured by ECHO or MUGA scan.

On completion of neoadjuvant chemotherapy and anti-HER2 treatment the following assessments will be performed:
1. Review of adverse events using CTCAE version 4.0
2. Clinical and radiological tumour measurement, which includes clinical measurement of breast tumour by calipers, radiological measurement of tumour(s) by ultrasound scan and mammogram
3. Axillary ultrasound will be performed and any abnormal nodes will be (re)sampled (by FNA or

biopsy) under image control
4. LVEF measurement by ECHO or MUGA
5. Blood sample collection for those patients taking part in the optional ctDNA substudy

Surgery: All patients will be scheduled for surgery after completing cycle 6 of neoadjuvant chemotherapy and anti-HER2 treatment. Surgery to the breast will be according to local protocol and finally determined after post-neoadjuvant Multidisciplinary Team meetings where all imaging and clinical factors will be reviewed. Appropriate surgical options will be discussed and agreed with patients as standard clinical practice. All patients must have either a SLNB or an axillary lymph node clearance as part of their surgical procedure post-neoadjuvant treatment unless a pre-neoadjuvant SLNB was successfully performed and was negative. Blood sample will be taken at the first clinic visit after surgery for those patients taking part in the optional ctDNA substudy.

Adjuvant anti-HER2 treatment (adjuvant trastuzumab): Traztuzumab will be continued following completion of neoadjuvant chemotherapy regimen. All patients will continue with adjuvant trastuzumab to receive a total of 18 cycles, +/- radiotherapy following surgery. Cardiac monitoring will continue during the administration of adjuvant trastuzumab.

Follow-up: Patient participation will end upon completion of surgery. Sites will be asked to provide follow-up information at 12 months from date of surgery. The 12 month follow-up will be performed in clinic face to face or via telephone assessments.

RESEARCH TIMETABLE:
Recruitment phase: It is anticipated that recruitment phase will take 18 months.
Follow-up: Follow-up at 12 months.

Planned final analysis: Analysis of the primary and available secondary outcomes will be performed once the last patient has completed surgery. Analysis of compliance to treatment will be performed once all patients have completed treatment and time to event analysis will be conducted once all patients have completed follow up.

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Previous interventions:

STUDY DESIGN:
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4. Review of adverse events. CTCAE version 4.0 will be used to grade adverse events.
5. Clinical tumour measurement (calipers): This is not required unless there is a concern or at discretion of the Investigator

End of Cycle 3 of neoadjuvant chemotherapy and anti-HER2 treatment: A clinical tumour assessment by caliper is mandatory to confirm absence of early disease progression at the end of cycle 3 (i.e. prior to commencing cycle 4 treatment). LVEF will also be measured by ECHO or MUGA scan.

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3. Axillary ultrasound will be performed and any abnormal nodes will be (re)sampled (by FNA or biopsy) under image control
4. LVEF measurement by ECHO or MUGA
5. Blood sample collection for those patients taking part in the optional ctDNA substudy

Surgery: All patients will be scheduled for surgery after completing cycle 6 of neoadjuvant chemotherapy and anti-HER2 treatment. Surgery to the breast will be according to local protocol and finally determined after post-neoadjuvant Multidisciplinary Team meetings where all imaging and clinical factors will be reviewed. Appropriate surgical options will be discussed and agreed with patients as standard clinical practice. All patients must have either a SLNB or an axillary lymph node clearance as part of their surgical procedure post-neoadjuvant treatment unless a pre-neoadjuvant SLNB was successfully performed and was negative. Blood sample will be taken at the first clinic visit after surgery for those patients taking part in the optional ctDNA substudy.

Adjuvant anti-HER2 treatment (adjuvant trastuzumab): Traztuzumab will be continued following completion of neoadjuvant chemotherapy regimen. All patients will continue with adjuvant trastuzumab to receive a total of 18 cycles, +/- radiotherapy following surgery. Cardiac monitoring will continue during the administration of adjuvant trastuzumab.

Follow-up: Patient participation will end upon completion of surgery. Sites will be asked to provide follow-up information at 12 months and 5 years from date of registration. The 12 month follow-up will be performed in clinic face to face. 5 year follow-up data will be collected in clinic face to face or via telephone assessments.

RESEARCH TIMETABLE:
Recruitment phase: It is anticipated that recruitment phase will take 18 months.
Follow-up: Follow-up at 12 months and at 5 years.

Planned final analysis: Analysis of the primary and available secondary outcomes will be performed once the last patient has completed surgery. Analysis of compliance to treatment will be performed once all patients have completed treatment and time to event analysis will be conducted once all patients have completed 5 years of follow up.

Intervention Type
Mixed

Primary outcome measure
1. The observed number of patients with false negative biopsies as a proportion of all those assessed will be reported as a proportion of all evaluable patients.
1.1. False negative biopsies are defined as the number of patients in which all core biopsies show no residual tumour but their surgical specimen does contain residual tumour.

Secondary outcome measures
1. Concordance between local and central histopathology reporting of pCR will be defined as the number of patients whose initial local pathological assessment of pCR is confirmed by Central Histopathology Review.
2. Compliance with neoadjuvant and adjuvant treatment; will be assessed by calculating relative dose intensity taking into account of both reductions in dose and delays to treatment.
3. Time to local recurrence; defined as time in whole days from date of registration to local recurrence or death from any cause. Patients who are alive and without local recurrence at the time of analysis will be censored at the date last seen.
4. Time to distant recurrence; defined in whole days from date of registration to distant recurrence or death from any cause. Patients who are alive and without distant recurrence at the time of analysis will be censored at the date last seen.
5. Overall survival; defined in whole days as the date of registration to death from any cause. Patients alive at the time of analysis will be censored at the date last seen.
6. Re-evaluation of the primary outcome using the Central Histopathological Review determination of RCB to define false negative biopsies as RCB-0 or 1 (no tumour or minimal residual disease) in the core biopsies but RCB-2 or 3 in the surgical specimen. This will be reported as a proportion of all recruited patients.
7. Ability of the axillary lymph node assessments post-neoadjuvant chemotherapy to identify definitive axillary lymph node involvement determined by surgery histopathology. Sensitivity, specificity and false negative rates will be reported.

Overall study start date
22/02/2016

Completion date
31/07/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/02/2022:

1. Patient with histological diagnosis of operable HER2-positive, ER-negative, early stage invasive breast cancer
2. Tumour size ≥1cm and visible on US (T1c to T4d)
3. Patient fit and willing to receive a NOSTRA-Feasibility Study approved treatment regimen in the opinion of the responsible clinician.
4. Eastern Co-operative Oncology Group (ECOG) performance status of 0 or 1
5. Women of child-bearing potential, prepared to adopt highly effective contraceptive measures if sexually active for at least 6 months after completion of study medication
6. Female, 18 years or older

7. Able to provide written informed consent for the study
8. Availability of embedded paraffin tumour blocks from pre-chemotherapy biopsy
9. The radiology team are able and willing to perform the tumour bed core biopsies
Additional Inclusion Criteria for ctDNA Sub-Study
1. Patient has not yet started neoadjuvant treatment.
2. Patient is willing and able to give blood samples as per ctDNA Sub-Study Guidelines

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Previous inclusion criteria:

1. Patient with histological diagnosis of operable HER2-positive, ER-negative, early stage invasive breast cancer
2. Tumour size ≥ 1cm and visible on US (T1c to T4d)
3. Patient fit and willing to receive one of the three planned NICE approved treatment regimens in the opinion of the responsible clinician
4. Eastern Co-operative Group (ECOG) performance status of 0 or 1
5. Women of childbearing potential, prepared to adopt highly effective contraceptive measures if sexually active for at least 6 months after completion of study medication
6. Female, aged ≥ 18 years
7. Able to provide written informed consent for the study
8. Availability of embedded paraffin tumour blocks from pre-chemotherapy biopsy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
150 participants, 30 hospitals

Key exclusion criteria
Current exclusion criteria as of 07/02/2022:

1. Previous ipsilateral invasive breast cancer or Ductal Carcinoma in Situ (DCIS)
2. Unequivocal evidence of distant metastatic disease at registration
3. Multi-focal disease at diagnosis
4. Active malignancy
5. Previous chemotherapy
6. Prior extensive radiotherapy (as judged by the Investigator) to bone marrow
7. Risk factors precluding the safe administration of the intended cytotoxic chemotherapy regimen
8. Patient unsuitable for the planned dual-targeted anti-HER2 treatment in opinion of the Investigator

9. Prior diagnosis of cardiac failure
10. Uncontrolled hypertension, coronary heart disease or other significant cardiac abnormality
11. Bleeding diathesis
12. Any evidence of other disease which in the opinion of the Investigator places the patient at high risk of treatment related complications
13. Pregnant (female patients of child bearing potential must have a urine or blood Human Chorionic Gonadotropin test performed to rule out pregnancy prior to study entry)
14. Patient lactating
15. Patients who have received live vaccine within 4 weeks of the date of study entry
16. Any concomitant medical or psychiatric problems which in the opinion of the Investigator would prevent completion of treatment or follow-up
17. Patient unfit and/or unwilling to undergo surgery
18. Patient unwilling or unable to comply with scheduled visits, treatment plan and study procedures
19. Patient has started protocol non-compliant neoadjuvant chemotherapy
20. Patient has started approved neoadjuvant chemotherapy but insufficient data is available to complete relevant CRFs
21. Patient has already received more than five cycles of approved neoadjuvant chemotherapy

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Previous exclusion criteria:

1. Previous invasive breast cancer
2. Unequivocal evidence of distant metastatic disease at registration
3. Active malignancy of non-breast origin
4. Previous chemotherapy
5. Prior extensive radiotherapy (as judged by the Investigator) to bone marrow
6. Risk factors precluding the safe administration of the intended cytotoxic chemotherapy regimen
7. Patient unsuitable for the planned dual-targeted anti-HER2 treatment in opinion of the Investigator
8. Prior diagnosis of cardiac failure
9. Uncontrolled hypertension, coronary heart disease or other significant cardiac abnormality
10. Bleeding diathesis
11. Any evidence of other disease which in the opinion of the Investigator places the patient at high risk of treatment related complications
12. Pregnant (female patients of child bearing potential must have a urine or blood Human Chorionic Gonadotropin test performed to rule out pregnancy prior to study entry)
13. Patient lactating
14. Patients who have received live vaccine within 4 weeks of the date of study entry
15. Any concomitant medical or psychiatric problems which in the opinion of the Investigator would prevent completion of treatment or follow-up
16. Patient unfit and/or unwilling to undergo surgery
17. Patient unwilling or unable to comply with scheduled visits, treatment plan and study procedures

Date of first enrolment
31/01/2019

Date of final enrolment

31/12/2023

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Singleton Hospital
Sketty Lane
Sketty
Swansea
United Kingdom
SA2 8QA

Study participating centre
Basildon
Basildon Hospital
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Borders General Hospital
Huntlyburn Terrace
Melrose
United Kingdom
TD6 9BS

Study participating centre
Belfast City Hospital
51 Lisburn Road

Belfast
United Kingdom
BT9 7AB

Study participating centre
Dumfries and Galloway Royal Infirmary
A75,
Cargenbridge
Dumfries
United Kingdom
DG2 8RX

Study participating centre
Llandough Hospital
Penlan Road,
Llandough
Penarth
United Kingdom
CF64 2XX

Study participating centre
Cheltenham General Hospital
Sandford Road
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Northwick Park Hospital
North West London Hospitals NHS Trust
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
Peterborough City Hospital
Edith Cavell Campus
Bretton Gate
Bretton
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Poole Hospital
Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre

Western General Hospital
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
Western Park Hospital
Whitham Road
Sheffield
United Kingdom
S10 2SJ

Study participating centre
Victoria Hospital
Blackpool Teaching Hospitals NHS Foundation Trust
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Arrowe Park Hospital
Arrowe Park Road
Wirral
United Kingdom
CH49 5PE

Study participating centre
Thomas Linacre Centre
Parsons Walk
Wigan
United Kingdom
WN1 1RU

Study participating centre
The Royal Marsden Hospital
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
St James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Royal Liverpool Hospital
Mount Vernon St
Liverpool
United Kingdom
L7 8YE

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
City Hospital NHS Trust
City Hospital N H S Trust
Dudley Road
Birmingham
United Kingdom
B18 7QH

Sponsor information

Organisation
University of Birmingham

Sponsor details
Dr Birgit Whitman
Head of Research Governance and Integrity
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United Kingdom
B15 2TT
+44 (0)121 415 8011
researchgovernance@contacts.bham.ac.uk

Sponsor type
University/education

Website
http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date

31/12/2025

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2.0	30/10/2018	21/01/2019	No	Yes
Participant information sheet	version 5.0	27/10/2020	22/06/2023	No	Yes
HRA research summary			28/06/2023	No	No