

Tailoring treatment for HER2-positive early breast cancer

Submission date 05/10/2021	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 11/10/2021	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 10/07/2025	Condition category Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-personalised-treatment-for-early-her2-positive-breast-cancer-her2-radical>

Background and study aims

Patients with the “HER2-positive” type of early breast cancer (HER2+ EBC) usually receive a course of drug treatment as well as surgery. This drug treatment improves chances of cure by destroying any breast cancer cells that might have already begun to spread. The aim is to reduce the burden of treatment and the risk of serious long-term side effects for some patients with HER2+ EBC. The researchers want to find out if they can adjust the amount of drug treatment given to patients after surgery according to the way the cancer initially responds to drug treatment before surgery.

Who can participate?

Patients aged 16 years and over with HER2+ EBC treated with neoadjuvant chemotherapy, pertuzumab and trastuzumab, who have a pathological complete response (pCR) at surgery.

What does the study involve?

Before entry into the study, a review of medical history and a pregnancy test (for all women who are able to get pregnant) will be conducted to determine if a patient is eligible to enter. Following study entry patients will continue to receive trastuzumab until a total of 9 cycles (about 6 months) of treatment have been given. This number of cycles includes the trastuzumab treatment received before entering the study. For patients who do not take part in the study it is likely that 17 or 18 cycles (about 1 year in total) of trastuzumab would be given. For some patients, the possibility of receiving pertuzumab and/or chemotherapy after surgery may have been discussed by their doctor, however, patients who have entered HER2-RADiCAL will not receive pertuzumab or any further chemotherapy after surgery. Patients will continue to receive trastuzumab in the same way that they would receive it if they were not taking part in the study. This may be as an injection under the skin or through a drip in the arm. During trastuzumab treatment the following assessments will be conducted. Before each cycle of trastuzumab the patient will have a discussion with their study doctor or nurse to document if there have been changes in their health since the last visit. Patients will continue to have their heart function measured with an echocardiogram (ECHO) or multiple gated acquisition (MUGA) scan in the

same way that would have happened if they were not taking part in the study. In many hospitals this will be done around 4 and 8 months after starting trastuzumab. Patients may receive other preventative treatments like hormone treatment, radiotherapy and bisphosphonates, just as they would if they were not taking part in this study. The study research team will request a sample of tumour tissue collected at the time of initial diagnosis and a copy of the pathology report. They will also ask for tissue samples (or images of tissue samples) collected at the time of surgery from about 100 study participants. These samples and images will be analysed by the research team to ensure that they agree with the diagnosis of pCR made by the hospital pathologist. About 30 days after the last cycle of trastuzumab, patients will have a discussion with their study doctor to document if there have been any changes in their health since the last visit. After treatment has finished, patients will have a mammogram and a follow up once a year for at least 5 years. The study research team also plan to collect routine information about the health of study participants, such as hospital admissions, information relating to their cancer, any treatments they might go on to receive and continued information about their overall health and wellbeing, from NHS databases.

What are the possible benefits and risks of participating?

By receiving a shorter duration of antibody treatment (trastuzumab and pertuzumab) and by not receiving adjuvant chemotherapy (if this had been discussed), patients may benefit from having fewer visits for treatment as well as a lower risk of short- and long-term side effects. Patients who take part in this study will be less likely to have some of these side effects because treatment is given for a shorter time.

By receiving less treatment patients may have a slightly increased risk of their cancer coming back. It is well known that patients who are suitable for this study have a high chance of remaining cancer-free with current treatment: about 96 in every 100 patients (96%) will remain free of cancer 3 years after diagnosis and about 94 in every 100 (94%) will remain cancer-free at 5 years from diagnosis. Based on previous research the study team think it is likely that carefully reducing treatment, as planned in this study, may not increase the risk of the cancer returning or may only increase the risk by a very small amount that could be balanced by the benefits of fewer side effects. However, this is not known for certain and this is why this research is being done. An independent group of scientists and doctors will closely monitor the progress and early results of the study to ensure that the continuation of the study remains safe and in the best interest of those patients volunteering to take part.

Where is the study run from?

The Institute of Cancer Research (ICR) (UK)

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

December 2019 to March 2032

Who is funding the study?

National Institute for Health Research – Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?

Katie Goddard

her2radical-icrctsu@icr.ac.uk

Study website

<https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/our-research/clinical-trials/her2-radical>

Contact information

Type(s)

Scientific

Contact name

Dr Katie Goddard

Contact details

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Additional identifiers

EudraCT/CTIS number

2021-001240-10

IRAS number

292122

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

CPMS 50425, IRAS 292122

Study information

Scientific Title

The HER2-RADiCAL study (Response ADaptive CAre pLan) – tailoring treatment for HER2 positive early breast cancer

Acronym

HER2-RADiCAL

Study objectives

HER2-RADiCAL seeks to test the hypothesis that a pathological complete response (pCR) to preoperative chemotherapy and anti-HER2 drug therapy can be used as a functional response biomarker to select patients who can safely receive less intensive personalised therapy, with minimal or no loss of efficacy in the population.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 20/08/2021, London - South East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8085; londonsoutheast.rec@hra.nhs.uk), REC ref: 21/LO/0529

Study design

Interventional non-randomized study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

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

Health condition(s) or problem(s) studied

HER2-positive early breast cancer

Interventions

Current interventions as of 21/12/2023:

Patients taking part in the study will continue treatment with trastuzumab until 9 cycles have been completed (rather than 18 cycles), including those cycles administered prior to study entry. No more pertuzumab will be given after study registration, and patients will not receive chemotherapy after surgery. Some patients may not receive a type of chemotherapy called an anthracycline if this was being deferred to after surgery. Any other treatment that might have been recommended (like hormone therapy or radiotherapy) will be given as normal.

Trastuzumab (original or biosimilar) should be given every 3 weeks to complete a total of 9 cycles including those cycles administered prior to study entry; the number of cycles given within the HER2-RADiCAL study is altered according to the number of cycles received prior to study entry. Trastuzumab may be administered via IV or subcutaneous routes in accordance with the standard practice at the site and will be administered as per the SmPC and local guidelines. Subcutaneous trastuzumab is administered at a dose of 600 mg every 3 weeks. Intravenous trastuzumab is administered at a dose of 6 mg/kg body weight every 3 weeks (with a loading dose of 8 mg/kg if required). No dose reductions are permitted.

Previous interventions:

Patients taking part in the study will continue treatment with trastuzumab until 9 cycles have been completed (rather than 18 cycles), including those cycles administered prior to study entry. No more pertuzumab will be given after study registration, and patients will not receive a type

of chemotherapy called an anthracycline, or any other type of chemotherapy, after surgery. Any other treatment that might have been recommended (like hormone therapy or radiotherapy) will be given as normal.

Trastuzumab (original or biosimilar) should be given every 3 weeks to complete a total of 9 cycles including those cycles administered prior to study entry; the number of cycles given within the HER2-RADiCAL study is reduced according to the number of cycles received prior to study entry. Trastuzumab may be administered via IV or subcutaneous routes in accordance with the standard practice at the site and will be administered as per the SmPC and local guidelines. Subcutaneous trastuzumab is administered at a dose of 600 mg every 3 weeks. Intravenous trastuzumab is administered at a dose of 6 mg/kg body weight every 3 weeks (with a loading dose of 8 mg/kg if required). No dose reductions are permitted.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Trastuzumab

Primary outcome measure

Relapse-free-interval (RFI), defined as time from registration to invasive local or distant relapse or death from breast cancer in the absence of a previously identified relapse (intercurrent deaths and second primary cancers censored). The primary timepoint of interest will be 3 years.

Secondary outcome measures

Efficacy:

1. Relapse-free-survival (RFS) defined as time from registration to invasive local or distant relapse or death from any cause (second primary cancers censored)
2. Invasive breast cancer-free survival (iBCFS) defined as time from registration to invasive local or distant relapse or ipsilateral or contralateral invasive second primary breast cancer (non-breast second primary cancers censored) or death from any cause
3. Invasive disease-free survival (iDFS) defined as time from registration to invasive local or distant recurrence, new invasive second cancer or death from any cause
4. Distant recurrence-free interval (DRFI) defined as time from registration to distant recurrence or death from any cause (second primary cancers and intercurrent deaths censored)
5. Breast cancer-free interval (BCFI) defined as time from registration to invasive local or distant relapse, or ipsilateral or contralateral invasive second primary breast cancer or DCIS or death from breast cancer in the absence of a previously identified relapse (intercurrent deaths and second primary cancers censored)
6. Overall survival defined as time from registration to death from any cause

Other:

1. Treatment pathway adherence: non-adherence is defined as the proportion of patients who receive >9 cycles of trastuzumab or who receive further adjuvant systemic anti-HER2 treatment (e.g. pertuzumab) or chemotherapy prior to recurrence or second primary
2. Cost-effectiveness: quality-adjusted life-years derived from a health economic model developed using clinical trial and real-world data at 3 and 5 years after study entry

Overall study start date

09/12/2019

Completion date

28/03/2032

Eligibility

Key inclusion criteria

Current inclusion criteria as of 21/12/2023:

1. Female or male, age ≥ 16 years
2. Histologically confirmed invasive breast cancer that is HER2-positive (IHC3+, and/or ISH positive/amplified) as determined by the local laboratory in accordance with national guidelines
3. Has received neoSACT chemotherapy with concomitant trastuzumab and pertuzumab
4. pCR (ypT0/is ypN0) in breast and sampled regional lymph nodes as per local pathology reporting
5. Imaging of breast and axilla prior to initiation of neoSACT and either:
 - 5.1. Breast primary radiological measurement ≤ 20 mm prior to neoSACT and limited nodal involvement (cN1) confirmed by axillary core biopsy or FNA (cT1N1)
- OR
- 5.2. Breast primary radiological measurement > 20 mm but ≤ 50 mm and node-negative (cT2N0) or limited nodal involvement (cT2N1)
6. Multiple ipsilateral cancers are permitted provided at least one meets the tumour size and axillary node inclusion criteria and none meet any of the exclusion criteria
7. Bilateral cancers are permitted provided at least one meets the tumour size and axillary node inclusion criteria and none meet any of the exclusion criteria
8. Pre-treatment diagnostic breast tumour biopsy sample available
9. Patient must be fit to continue treatment with trastuzumab and have no concomitant medical, psychiatric or social problems that might interfere with informed consent, adherence to the reduced treatment pathway or follow-up
10. Provision of written informed consent to participate in HER2-RADiCAL

Previous inclusion criteria:

1. Female or male, age ≥ 16 years
2. Histologically confirmed invasive breast cancer that is HER2-positive (IHC3+, and/or ISH positive/amplified) as determined by the local laboratory in accordance with national guidelines
3. Has received neoSACT with a non-anthracycline chemotherapy regimen with at least 3 cycles of concomitant trastuzumab and pertuzumab
4. pCR (ypT0/is ypN0) in breast and sampled regional lymph nodes as per local pathology reporting
5. Imaging of breast and axilla prior to initiation of neoSACT and either:
 - 5.1. Breast primary radiological measurement ≤ 20 mm prior to neoSACT and limited nodal involvement (cN1) confirmed by axillary core biopsy or FNA (cT1N1)
- OR
- 5.2. Breast primary radiological measurement > 20 mm but ≤ 50 mm and node-negative (cT2N0) or limited nodal involvement (cT2N1)
6. Multiple ipsilateral cancers are permitted provided at least one meets the tumour size and axillary node inclusion criteria and none meet any of the exclusion criteria
7. Bilateral cancers are permitted provided at least one meets the tumour size and axillary node inclusion criteria and none meet any of the exclusion criteria
8. Pre-treatment diagnostic breast tumour biopsy sample available

9. Study consent ≤ 6 weeks after completing breast cancer surgery
10. Patient must be fit to continue treatment with trastuzumab and have no concomitant medical, psychiatric or social problems that might interfere with informed consent, adherence to the reduced treatment pathway or follow-up
11. Provision of written informed consent to participate in HER2-RADiCAL

Participant type(s)

Patient

Age group

Adult

Lower age limit

16 Years

Sex

Both

Target number of participants

Planned Sample Size: 720; UK Sample Size: 720

Key exclusion criteria

Current exclusion criteria as of 21/12/2023:

1. Evidence of metastatic disease at any time since diagnosis
2. Any residual invasive disease following neoSACT. This includes isolated tumour cells in axillary nodes or tissue or evidence of lymphovascular invasion in the breast. Persistent ductal or lobular non-invasive disease (DCIS or LCIS) is permitted. Resection margins must be deemed clear of any residual DCIS according to local MDT protocol
3. Breast-conserving primary surgery where it is known that breast irradiation will not be administered (e.g. due to contraindication or patient preference)
4. Intraoperative assessment of post-neoSACT axillary SLN using one-stop nucleic acid amplification (OSNA)
5. Any planned further resectional surgery for breast cancer (including re-excision, mastectomy, or axillary surgery)
6. HER2-negative invasive breast carcinoma
7. Breast cancer with clinical stage of $T \geq 3$ at diagnosis
8. Evidence of scarring (or other pathological features consistent with previous malignant involvement) in >4 axillary nodes or clinical nodal stage $N \geq 2$ at any time
9. Positive SLNB pre-neoadjuvant systemic therapy as this precludes determination of pCR
10. Pregnant and/or lactating women
11. Female patient of child-bearing potential, unwilling to use an effective form of contraception during trastuzumab treatment and for 7 months after their last dose of trastuzumab
12. Previous diagnosis of invasive breast carcinoma
13. Previous diagnosis of any other (non-breast) malignancy unless disease-free for at least 5 years and considered to be at low risk of recurrence or treated basal cell or localised squamous cell carcinoma of the skin or cervical intraepithelial neoplasia
14. Chemotherapy administered following surgery (NB. Pertuzumab and/or trastuzumab may have been continued after surgery as per local practice prior to study entry)
15. Has received >9 cycles trastuzumab. In the event a patient has received 9 cycles prior to study entry then consent must occur within 3 weeks of the last dose of trastuzumab.
16. Clinically significant cardiac disease within 12 months of starting trastuzumab, including

unstable angina, acute myocardial infarction, New York Heart Association Class III or IV congestive heart failure, cerebral vascular accident, or cardiac arrhythmia associated with haemodynamic instability

17. Left ventricular ejection fraction (LVEF) less than 50% on most recent cardiac imaging

18. History of interstitial lung disease

19. Any medical or other contra-indication to continuing trastuzumab

Previous exclusion criteria:

1. Evidence of metastatic disease at any time since diagnosis

2. Any residual invasive disease following neoSACT. This includes isolated tumour cells in axillary nodes or tissue or evidence of lymphovascular invasion in the breast. Persistent ductal or lobular non-invasive disease (DCIS or LCIS) is permitted. Resection margins must be deemed clear of any residual DCIS according to local MDT protocol

3. Any planned further resectional surgery for breast cancer (including re-excision, mastectomy, or axillary surgery)

4. HER2-negative invasive breast carcinoma

5. Breast cancer with clinical stage of T \geq 3 at diagnosis

6. Evidence of scarring (or other pathological features consistent with previous malignant involvement) in >4 axillary nodes or clinical nodal stage N \geq 2 at any time

7. Positive SLNB pre-neoadjuvant systemic therapy as this precludes determination of pCR

8. Pregnant and/or lactating women

9. Female patient of child-bearing potential, unwilling to use an effective form of contraception during trastuzumab treatment and for 7 months after their last dose of trastuzumab

10. Previous diagnosis of invasive breast carcinoma

11. Previous diagnosis of any other (non-breast) malignancy unless disease-free for at least 5 years and considered to be at low risk of recurrence or treated basal cell or localised squamous cell carcinoma of the skin or cervical intraepithelial neoplasia

12. Chemotherapy administered following surgery (NB. Pertuzumab and/or trastuzumab may have been continued after surgery as per local practice prior to study entry)

13. Has received >9 cycles trastuzumab

14. Any medical or other contra-indication to continuing trastuzumab

Date of first enrolment

03/12/2021

Date of final enrolment

30/11/2027

Locations

Countries of recruitment

England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
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United Kingdom
EH1 3EG

Study participating centre
Belfast City Hospital
Lisburn Road
Belfast
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BT9 7AB

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
The Maidstone Hospital
Hermitage Lane
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ME16 9QQ

Study participating centre
Royal Free Hospital
Pond Street
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NW3 2QG

Study participating centre
Queens Medical Centre
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Nottingham
United Kingdom
NG7 2UH

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

Study participating centre
Colchester Dist General Hospital
Turner Road
Colchester
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CO4 5JL

Study participating centre
Ysbyty Gwynedd
Penrhosgarnedd
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LL57 2PW

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

Study participating centre

Royal Cornwall Hospital

Treliske

Truro

United Kingdom

TR1 3LJ

Study participating centre

Poole Hospital

Longfleet Road

Poole

United Kingdom

BH15 2JB

Study participating centre

Kent & Canterbury Hospital

Ethelbert Road

Canterbury

United Kingdom

CT1 3NG

Study participating centre

St Thomas' Hospital

Westminster Bridge Road

London

United Kingdom

SE1 7EH

Study participating centre

Christie Hospital

550 Wilmslow Road

Withington

Manchester

United Kingdom

M20 4BX

Study participating centre

Medway Maritime Hospital

Windmill Road

Gillingham

United Kingdom

ME7 5NY

Study participating centre

NHS Borders

Newstead

Melrose

United Kingdom

TD6 9DB

Study participating centre

Queen Elizabeth Hospital

Gayton Road

King's Lynn

United Kingdom

PE30 4ET

Study participating centre

St Mary's Hospital

South Wharf Road

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W2 1BL

Study participating centre

Worcestershire Royal Hospital

Charles Hastings Way

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WR5 1DD

Study participating centre

Northern General Hospital

Herries Road

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United Kingdom

S5 7AU

Study participating centre

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1053 Great Western Road

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United Kingdom
G12 0YN

Study participating centre
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Study participating centre
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TN24 0LZ

Study participating centre
Queen Elizabeth the Queen Mother Hospital
St. Peters Road
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CT9 4AN

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

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
Bristol Haematology and Oncology Center
22 Horfield Rd
Bristol
United Kingdom
BS2 8ED

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

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

Study participating centre
Royal Lancaster Infirmary
Ashton Road
Lancaster
United Kingdom
LA1 4RP

Study participating centre
Westmorland General Hospital
Burton Rd
Kendal
United Kingdom
LA9 7RG

Study participating centre

Furness General Hospital

Dalton Lane
Barrow-in-furness
United Kingdom
LA14 4LF

Study participating centre**Clatterbridge Cancer Centre**

65 Pembroke PLACE
Liverpool
United Kingdom
L7 8YA

Study participating centre**St Mary's Hospital**

St. Marys Hospital
Parkhurst Road
Newport
United Kingdom
PO30 5TG

Study participating centre**Glan Clwd Hospital**

Ysbyty Glan Clwydd
Bodelwyddan
Rhyl
United Kingdom
LL18 5UJ

Study participating centre**Wrexham Maelor Hospital**

Croesnewydd Road
Wrexham Technology Park
Wrexham
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LL13 7TD

Study participating centre**Weston Park Hospital**

Whitham Rd
Broomhall

Sheffield
United Kingdom
S10 2SJ

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
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AB25 2ZN

Study participating centre
West Middlesex University Hospital
Twickenham Road
Isleworth
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TW7 6AF

Study participating centre
Weston General Hospital
Grange Road
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BS23 4TQ

Study participating centre
Uclh
250 Euston Road
London
United Kingdom
NW1 2PQ

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
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EX2 5DW

Study participating centre**Maidstone**

Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

Study participating centre**Northampton General Hospital**

Cliftonville
Northampton
United Kingdom
NN1 5BD

Sponsor information**Organisation**

Institute of Cancer Research

Sponsor details

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Barbara.Pittam@icr.ac.uk

Sponsor type

Research organisation

ROR

<https://ror.org/043jzw605>

Funder(s)**Funder type**

Government

Funder Name

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: .

Results and Publications

Publication and dissemination plan

1. The study protocol is available online at <https://fundingawards.nihr.ac.uk/award/NIHR131362>
2. The main study results will be published in a peer-reviewed journal, on behalf of all collaborators. The manuscript will be prepared by a writing group, consisting of members of the Trial Management Group. Participating clinicians may be selected to join the writing group on the basis of intellectual and time input. All participating clinicians will be acknowledged in the publication. Additional documents are not available at this time.

Intention to publish date

30/11/2030

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be available on request from the HER2-RADiCAL trial team via her2radical-icrctsu@icr.ac.uk via completion of a data access request form after such time that the primary analysis publication and any other key analyses have been completed. Optional advanced consent/authorisation for the possible future sharing of information collected about patients will be obtained at study entry.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.0	11/10/2021	16/05/2022	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 4.0	24/02/2023	21/12/2023	No	No