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Tailoring treatment for HER2-positive early breast cancer

Submission date 05/10/2021	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 11/10/2021	**Overall study status** Ongoing	
Last Edited 10/07/2025	**Condition category** Cancer	

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
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2021-001240-10

Integrated Research Application System (IRAS)
292122

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Treatment

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(s)
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.

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
All

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≥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≥2 at any time9. 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

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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
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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
United Kingdom

England

Northern Ireland

Scotland

Wales

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

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place

Edinburgh
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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
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Queens Medical Centre
Derby Road
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NG7 2UH

Study participating centre
Yeovil District Hospital
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Study participating centre
Colchester Dist General Hospital
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NHS Forth Valley
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United Kingdom
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United Kingdom
TR1 3LJ

Study participating centre
Poole Hospital
Longfleet Road
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BH15 2JB

Study participating centre
Kent & Canterbury Hospital
Ethelbert Road
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CT1 3NG

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
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SE1 7EH

Study participating centre
Christie Hospital
550 Wilmslow Road
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M20 4BX

Study participating centre
Medway Maritime Hospital
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ME7 5NY

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Study participating centre

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Worcestershire Royal Hospital
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CT9 4AN

Study participating centre
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W6 8RF

Study participating centre
Bristol Haematology and Oncology Center
22 Horfield Rd
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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
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DG2 8RX

Study participating centre
Royal Lancaster Infirmary
Ashton Road
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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
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PO30 5TG

Study participating centre
Glan Clwd Hospital
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Bodelwyddan
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LL18 5UJ

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Wrexham Maelor Hospital
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LL13 7TD

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Maidstone
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Study participating centre

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Sponsor information

Organisation
Institute of Cancer Research

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

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?
HRA research summary			28/06/2023	No	No
Protocol file	version 2.0	11/10/2021	16/05/2022	No	No
Protocol file	version 4.0	24/02/2023	21/12/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes