To be printed on hospital headed paper

The HER2-RADiCAL Study (Response ADaptive CAre pLan) – Tailoring Treatment for HER2-Positive Early Breast Cancer

POST-SURGERY PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM
Version 4.0, 01 September 2023

Invitation to take part in a research study

- You are being invited to take part in a research study called HER2-RADiCAL.
- Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve.
- In this information sheet you will be able to find details on why the study is being done, why you have been invited to take part and what will be involved if you decide to take part.
- Please take time to read this information sheet carefully and discuss it with friends, relatives and your GP if you wish.
- Please ask your study doctor or nurse if there is anything that is not clear or if you would like more information.
- Please take as much time as you need to decide whether or not you wish to take part in the HER2-RADiCAL study.
- Your participation is entirely voluntary. If you decide not to take part this will not affect your standard of care or any future care you will get.
- If you have private medical insurance, please check with the insurance company that taking part in this study will not affect your policy.
- If you decide to take part, you will be asked to sign the consent form at the end of this information sheet. You will be given a copy of this information sheet and a signed consent form to take home with you.
- Even after you have signed the consent form, you can change your mind at any time and withdraw from the study. You do not have to give a reason.

A research study sponsored and co-ordinated by:

ICR The Institute of Cancer Research

REC Ref: 21/LO/0529; IRAS Project ID: 292122; EudraCT: 2021-001240-10; CCR number: CCR5408

Why is this study being conducted and what does it involve?

- The HER2-RADiCAL study is for patients with HER2-positive early breast cancer, who:
    - have started their course of drug treatment (chemotherapy + trastuzumab + pertuzumab) before surgery
    - have now had breast surgery
    - have been found to have the best possible response to treatment (this is called a "pathological complete response" or "pCR", and this means that no living cancer cells remain in any of the tissue that was removed at surgery)

- It is already known that patients with the above characteristics have only a small chance of their cancer returning and so it is possible that the side effects and risks of continuing some treatments could outweigh any benefit.

- The study will investigate whether a more personalised treatment plan can be offered. The aim is to find out if patients with a pCR can safely receive less drug treatment after surgery, reducing unnecessary side effects, and still have the same high chance of cure.

- If you take part in the study you will continue treatment with trastuzumab until you have completed 9 cycles (including those you have already received). You will not receive any more pertuzumab or chemotherapy.

- All other treatments that might have been recommended (such as hormone therapy or radiotherapy) will still be given, just as if you were not taking part in the study.

- If you take part in this study you will be asked to donate some tissue samples for use in research. These tissue samples will have already been removed during biopsy procedures or surgery. No new tissue samples will need to be taken.

- Information about your health will be provided to the study research team by you, and by your local hospital team, during and after treatment in order to undertake this study. National records, which are kept on everyone's health status, will also be used by the study research team to find out how you are getting on.

- All information about you which is collected during the study will be kept strictly confidential and will be stored securely.

HER2-RADiCAL PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM

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Part One: About the HER2-RADiCAL study

What is the purpose of the HER2-RADiCAL study?

Doctors offer a combination of chemotherapy and antibody drugs to patients with HER2-positive early breast cancer. This is to reduce the risk of the cancer returning after breast surgery and is usually very effective.

The treatments used today were developed over many years. As new drugs were discovered these were added to the existing treatments to improve the chance of patients remaining cancer-free. This means that the treatments given to patients now are made up of a combination of several different drugs that are given over many months. These combination drug treatments are effective, but also cause side effects.

Based on research that has already been done, it is now known that every part of this combination treatment might not be needed for every patient. More is also known about the downsides from drug treatments. These include the short and long-term side effects of the treatment as well as other issues like frequent visits to the hospital that can delay return to normal life.

In recent years it has become standard practice to start the drug treatments for HER2-positive early breast cancer before breast surgery. This gives doctors the opportunity to measure how well the drug treatment given before surgery has worked for each patient. Doctors are starting to use this result to develop a more personalised plan for the remaining part of each patient's treatment given after surgery.

The HER2-RADiCAL study will investigate whether patients that have had the best possible response to treatment (pCR) can safely receive less drug treatment after surgery whilst keeping the chance of their cancer returning very small.

Why am I being invited to take part?

Your oncologist believes you may be suitable to take part in this study because you are currently having treatment for HER2-positive early breast cancer. Your treatment so far has included chemotherapy and two antibody drugs (called "trastuzumab" and "pertuzumab"), followed by breast surgery.

Tests on your tissue removed at surgery have shown that your cancer has had an excellent response to the drug treatment you received before your operation. A pathologist has examined your tissue with a microscope, and they could not find any living cancer cells in any of the tissue that was removed. This is called a "pathological complete response" (shortened to "pCR"). Patients with your type of cancer who have this excellent response have only a small chance of the cancer coming back.

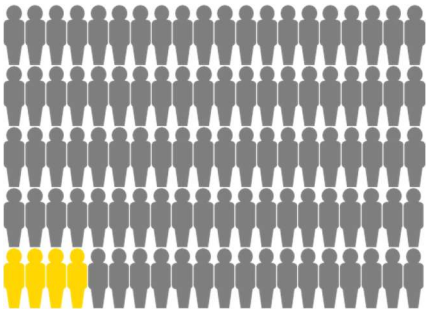
The HER2-RADiCAL study is taking place at NHS hospitals across the UK and aims to recruit 720 patients with HER2-positive early breast cancer who have had a pCR at surgery.

What is the idea behind the HER2-RADiCAL study?

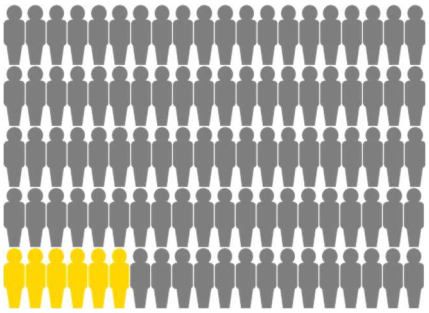
The idea behind HER2-RADiCAL is to adapt the treatment given after surgery for patients who have had an excellent response (a pCR) to the treatment they received before surgery. Patients who have a pCR are known to have a very good chance of remaining free of their cancer. Previous research studies have shown that around 94 out of every 100 patients (94%) with a pCR would remain free of cancer 5 years after diagnosis with the treatment given currently. It is uncommon for this type of breast cancer to return later than this.

The risk of cancer returning 3 and 5 years after diagnosis

Around 96 out of every 100 women would remain free of their cancer in 3 years' time. This means that the cancer may come back in 4 out of 100 women over **3 years**.



Around 94 out of every 100 women would remain free of their cancer in **5 years'** time. This means that the cancer may come back in 6 out of 100 women over **5 years**.



The aim of HER2-RADiCAL is to find out if patients with a pCR can safely receive less drug treatment after surgery. By receiving less treatment there may be a slightly increased chance of a patient's cancer coming back, however we do not know for certain whether this will be the case or not.

In a previous research study, called the PERSEPHONE trial (see 'further reading' section for more detail) patients were treated with 6 months of trastuzumab or 12 months of trastuzumab. The patients who received 6 months of trastuzumab in the trial had no greater risk of the cancer returning than patients treated with 12 months of trastuzumab.

Based on previous research including the results of the PERSEPHONE trial, we expect that carefully reducing some parts of the treatment given after surgery in patients who have had a pCR:

- is unlikely to lead to an increased risk of a patient's cancer coming back, and
- will spare patients the side effects and disadvantages of a longer course of treatment.

This idea now needs to be tested before it can become standard treatment for patients treated in the NHS.

Do I have to take part?

It is up to you to decide whether or not to take part in this study. Your participation is entirely voluntary, and you will be given sufficient time to decide if you wish to participate. The standard of care you receive will not be affected by your decision to take part, or not take part, in the HER2-RADiCAL study. If you do agree to participate in the study, you are free to decide to end your participation at any time. You do not have to give a reason.

What will happen if I decide to take part?

If you decide to take part, you will be given this information sheet to take home and you will be asked to sign a consent form. After you have agreed to take part by signing the consent form, your study doctor will review your medical history to check that you are eligible to enter the study. A pregnancy test will be carried out for all women who are able to get pregnant as there are risks associated with pregnancy in patients receiving trastuzumab treatment. If you are pregnant you will not be able to enter this study.

If you are eligible, you will be registered for the study. If however you are not suitable or you decide you do not want to participate in this study your study doctor will discuss the treatment options available outside of this study with you.

The study research team will ask your hospital for a sample of your tumour tissue collected at the time of your initial diagnosis and a copy of your pathology report. They will also ask for tissue samples collected at the time of surgery from approximately 100 study participants. These samples will be analysed by the research team to ensure that they agree with the diagnosis of pCR made by the hospital pathologist. In the unlikely event that the research team disagree with the diagnosis of pCR your case will be reviewed by the research and hospital pathologists and your study doctor will discuss this with you.

Once you have been registered for the study you will be provided with a questionnaire booklet that asks about your general health and how your diagnosis and treatment has affected your daily life. This is called a 'patient reported outcomes' questionnaire. A member of your medical team will explain the questionnaire before you complete it and answer any questions that you have. The questionnaire should take about 10 minutes to complete.

What treatment will I receive?

If you agree to take part in the HER2-RADiCAL study, you will continue to receive trastuzumab until you have received a total of 9 cycles (about 6 months) of treatment. This number of cycles includes the trastuzumab treatment that you have already received before joining the study. If you do not take part in the study, it is likely that you will receive trastuzumab for 17 or 18 cycles (about 1 year in total).

For some patients, your doctor may have initially discussed with you the possibility of receiving pertuzumab and/or chemotherapy after your surgery. If you take part in this study, you will not receive any further pertuzumab. You will not receive any further chemotherapy after your surgery. Your doctor will be able to discuss with you exactly how the treatment that you would receive if you take part in the study differs from the treatment that you would receive if you do not participate.

Your doctor may also have recommended other preventative treatments like hormone treatment, radiotherapy and bisphosphonates. These treatments will still be given just as if you were not taking part in the HER2-RADiCAL study.

How is trastuzumab treatment given?

Trastuzumab may be given 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 you will have a discussion with your study doctor or nurse to document if there have been changes in your health since your last visit.
- You will continue to have your heart function measured with an echocardiogram (ECHO) or multiple gated acquisition (MUGA) scan in the same way that would have happened if you were not taking part in the study. In many hospitals this will be done around 4 and 8 months after starting trastuzumab.

Will I be able to have a COVID-19 vaccination while I am receiving trastuzumab treatment?

Currently available COVID-19 vaccines (Pfizer/BioNTech, Oxford University/AstraZeneca and Moderna) are permitted. If any further COVID-19 vaccines become available, your study doctor will

be able to advise you as to whether these vaccines are permitted while you are receiving trastuzumab treatment within the study.

What will happen once I finish trastuzumab treatment?

About 30 days after your last cycle of trastuzumab, you will have a discussion with your study doctor to document if there have been any changes in your health since your last visit and you will be sent a follow up patient reported outcomes questionnaire booklet for you to complete about your general health and how your treatment has affected your daily life.

After your treatment has finished, your study doctor will assess your progress and you will have a mammogram once a year for at least 5 years. You may be asked to come to the hospital for the follow up visits or, with your agreement, you may be contacted by phone or email instead. You will be sent the same follow up patient reported outcomes questionnaire booklet about your general health and how your treatment has affected your daily life, once a year for up to 5 years. The follow up questionnaires will be sent to your home address and before we send them out we will check with your GP and/or hospital doctor that you are well.

The study research team also plan to collect routine information about your health, such as hospital admissions, information relating to your cancer, any treatments you might go on to receive and continued information about your overall health and wellbeing, from NHS databases. Anonymised copies of any scans which are conducted as part of your routine care may also be collected.

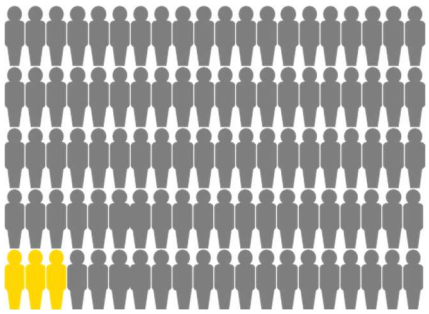
If you have any concerns during or after trastuzumab treatment, you may request a visit with your study doctor to assess any signs or symptoms that you are worried about.

What are the possible benefits of taking part?

By receiving a shorter duration of antibody treatment (trastuzumab and pertuzumab) you may benefit from having fewer visits for treatment as well as a lower risk of side effects.

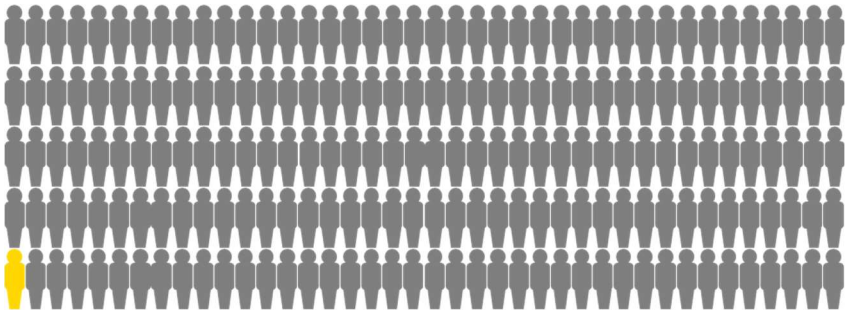
Your doctor will already have discussed the possible side effects of trastuzumab and pertuzumab with you before you started treatment. Patients who take part in this study will be less likely to have some of these side effects because treatment is given for a shorter time. For example, a recent research study called PERSEPHONE found that heart problems (including symptoms of breathlessness or fluid retention caused by the heart not pumping properly, or needing to start heart medication) were seen in 11 of every 100 patients (11%) who received trastuzumab for 1 year compared to 8 of every 100 patients (8%) who received trastuzumab for 6 months.

Avoiding heart problems by receiving a shorter duration of trastuzumab
In patients receiving 12 months of antibody treatment, around 11 out of 100 patients will experience heart problems. However, in patients receiving 6 months of antibody treatment, around 8 out of 100 patients will experience heart problems. Therefore 3 out of 100 patients may avoid heart problems by receiving a shorter duration of trastuzumab.



Some less serious symptoms such as cough, palpitations, tiredness, chills, muscle or joint pain and nausea were also less common in patients receiving trastuzumab for 6 months rather than 12 months.

Avoiding diarrhoea caused by long-term pertuzumab treatment
Around 1 in 200 patients who continue to receive pertuzumab after chemotherapy may develop severe diarrhoea (bad enough that inpatient hospital treatment could be required).

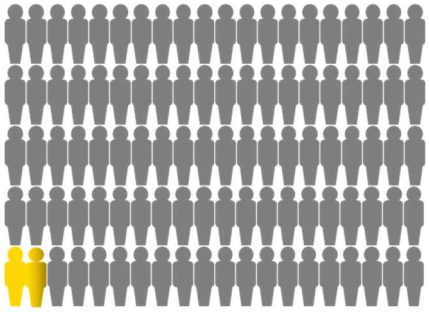


If you enter the trial, then you will not receive any more pertuzumab and so the risk of developing severe diarrhoea is reduced.

If you have already finished your planned course of chemotherapy before surgery then taking part in HER2-RADiCAL will make no difference to the chemotherapy part of your treatment. However, if your treatment plan involved receiving a type of chemotherapy drug called an anthracycline after your surgery then you will no longer receive this. Ask your doctor if you are not sure if this applies to you.

The most commonly used anthracycline drugs are called doxorubicin and epirubicin. The side effects during anthracycline treatment include hair loss, nausea and vomiting (which is usually well controlled with anti-sickness medication) and a weakened immune system. Longer-term side effects (occurring several years after the anthracycline was given) are uncommon but can be serious. These longer-term side effects include heart problems caused by chemotherapy damage to the heart muscle.

Long-term heart problems caused by anthracycline chemotherapy
In patients receiving chemotherapy containing an anthracycline, 1-2 patients in every 100 (1-2%) may develop symptoms of breathlessness or fluid retention caused by the heart not pumping properly. By not continuing chemotherapy after surgery, the risk of developing long-term heart problems is reduced.



Anthracyclines also increase the risk of developing leukaemia. This risk is thought to be up to 1 in 300 (in other words if 300 patients received an anthracycline, 1 of them would later develop leukaemia). By not continuing chemotherapy after surgery and thus not receiving chemotherapy containing an anthracycline, this risk of developing leukaemia is reduced.

Anthracycline drugs are commonly used in the treatment of breast cancer and their benefits are considered to outweigh these risks. However, this might not be the case in a patient who has already had a pCR and this is why they are being avoided in patients who have agreed to take part in HER2-RADiCAL.

You can take part in HER2-RADiCAL if you have already received an anthracycline drug as part of your treatment before surgery.

The research team cannot be certain the study will help you, but any information gained from this study will help researchers to develop better treatment options for future patients with HER2-positive early breast cancer.

What are the possible disadvantages and risks of taking part?

By receiving less treatment than you would if you continued to receive standard treatment, you may have a slightly increased risk of your cancer coming back. Evidence shows that for that patients who are suitable for this study have a high chance of remaining cancer-free. 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 research 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, we do not know this 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 HER2-RADiCAL study to ensure that continuation of the study remains safe and in the best interest of those patients volunteering to take part. If the study is stopped for any reason your study doctor will discuss with you the treatment options available. This may include continuing or re-starting antibody treatment to complete 1 year, which is the treatment you would receive if you were not taking part in the HER2-RADiCAL study.

During this study you will continue to have your heart function measured with an echocardiogram (ECHO) or MUGA scan, and you may also have electrocardiograms (ECGs) to assess your heart rhythm, in the same way that would have happened if you were not taking part in the study. ECGs involve placing small electrodes on the surface of your skin. Occasionally, a slight redness or inflammation may appear due to the adhesives used to attach the electrodes to the skin. After your treatment you will have a mammogram once a year for at least 5 years as part of your routine care. If you take part in this study you will not undergo any additional scans or mammograms over and above those you would have as part of your standard care outside of the study. Mammograms and MUGA scans use ionising radiation to form images of your body and provide your doctor with clinical information. Ionising radiation can have an adverse effect on the body, including a small increased risk of causing a cancer many years or decades after the exposure. The chances of this happening to you are the same whether you take part in this study or not.

There are risks associated with pregnancy and breastfeeding in patients receiving trastuzumab treatment and in patients undergoing mammograms and MUGA scans. Therefore, if you could potentially become pregnant you will need to have a pregnancy test before joining this study and if you are pregnant or breastfeeding you will not be able to enter. You may also have pregnancy tests during your treatment and if you become pregnant while receiving trastuzumab, these risks could affect you or your unborn child. If applicable, you must continue using adequate birth control during trastuzumab treatment and for at least 7 months after stopping treatment. If you think you may be pregnant while receiving trastuzumab, you must tell your study doctor immediately and, if you are due to undergo a MUGA scan, you must inform the staff who will be performing the scan immediately. If you think you may be pregnant at the time of your annual mammogram appointments, please inform the staff due to perform the mammogram. Pregnancy will be a reason to stop trastuzumab treatment. If you become pregnant, information on the outcome of your pregnancy will be requested.

What will happen if my cancer comes back whilst I am taking part in the study?

If your cancer comes back whilst you are taking part in the study, your doctor will discuss with you the treatment options available. As part of standard care at your hospital you may have a biopsy or surgery to remove part, or all of the tumour that has come back. If you have given your agreement, the study research team will ask your hospital for a sample of this tumour tissue so that it can be compared against the sample collected at the time of your diagnosis. This will be used to help the research team study why breast cancer still returns in a small number of patients even after a pCR. This research may help future patients but it will not provide information directly relevant to your care.

Part Two: General information

Who is organising and funding the research?

The research study is being carried out by a network of doctors across the UK. The study is sponsored and co-ordinated by The Institute of Cancer Research (ICR). The research is approved and funded by the National Institute for Health Research – Health Technology Assessment (HTA) Programme. Your study doctor will not receive any payments for including you in this research study.

Who will have access to my data

The Institute of Cancer Research is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The Institute of Cancer Research will keep identifiable information about you for at least 5 years after the study has finished.

The Institute of Cancer Research's lawful basis for processing your information is for the performance of a task carried out in the public interest and it is necessary to process sensitive health and genetic information for the purposes of scientific research with appropriate safeguards in place to protect personal information, as required by the United Kingdom General Data Protection Regulation (UK GDPR).

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/transparency

[Insert appropriate name for NHS site] will collect information from you and your medical records for this research study in accordance with our instructions.

[Insert appropriate name for NHS site] will use your full name, hospital number, date of birth, postcode and NHS number (or Community Health Index (CHI) and/or hospital number in Scotland) to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study.

Will my taking part in this study be kept confidential?

All information which is collected about you during the study will be kept strictly confidential. When you join the trial, your full name, hospital number, date of birth, postcode and NHS/CHI number will be passed to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the study is being coordinated. You will be given a unique trial ID number, which will be used together with your initials and date of birth on forms that the research staff at your hospital will send to ICR-CTSU. All information about you will be stored securely. It will be treated as strictly confidential and nothing that might identify you will be revealed to any third party. Only members of the research teams at your hospital and the ICR-CTSU will have access to the information that could allow this trial ID number to be linked to you.

From time to time, we would like to know how you are getting on. Ideally, we would like to do this for life, and we would like to use national records, which are kept on everyone's health status to find this out. One of these is held at the General Register Office (GRO). We will need to give them enough information to identify you. This is usually your name, date of birth, postcode and NHS number (or Community Health Index (CHI) and/or hospital number in Scotland). Any details we receive from any source are confidential and will only be used for the purposes of the trial. Please initial the consent form to show that we have your permission to do this.

Representatives from the ICR-CTSU, the NHS Trust relevant to your taking part in research, the Medicines and Healthcare products Regulatory Agency (MHRA) and third parties approved by ICR-CTSU may need to see your hospital or clinic records to the extent permitted by applicable laws and regulations to make sure the information received is correct. All information will be kept confidential.

[Insert appropriate name for NHS site] will keep identifiable information about you from this study for at least 5 years after the study has finished.

Will information about me be shared with other researchers?

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations now or in the future. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

Our main privacy policy can be found at https://www.icr.ac.uk/legal/privacy. If you have any questions about your rights under the GDPR or how we use your information please contact our Data Protection Officer at dataprotectionofficer@icr.ac.uk.

What are my choices about how my information is used?

You can stop taking part in the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage our records in specific ways for the research to be reliable and accurate. This means that your rights to access, change or move your information is limited. To safeguard your rights, we will use the minimum personally-identifiable information possible.

What will happen to any samples I give?

The group of medical professionals overseeing the HER2-RADiCAL study will also oversee the storage and use of tissue samples. Your tumour tissue samples may be labelled with your initials, date of birth, your unique Study ID number, date of sample collection, and pathology number when they are sent to the HER2-RADiCAL research laboratory. When they arrive at the laboratory they will be coded and personal details removed to maintain your confidentiality. Digital pictures of your tissue samples may be taken and stored on secure computers. These images will be labelled with your unique Study ID number only.

The tumour samples and images will be stored securely at laboratories at The University of Birmingham and The Institute of Cancer Research. Surplus tumour material will be stored indefinitely at The University of Birmingham laboratory, The Institute of Cancer Research or an off-site (UK based) approved storage facility. You are asked to give permission for possible future research using these samples and sample images; this may involve your samples and sample images being sent to institutions outside the UK and the European Economic Area. The confidential nature of these samples, images and associated data will be fully protected, and any other research using your tissue will first be reviewed and approved by an ethics committee.

With your agreement, the samples you donate may be used in the future for analysis that may include genetic analysis. The results of these tests will not be made available to you or your doctor. There is always a theoretical possibility that your identity could be picked out from the results of your sample analysis, even without identifiers. This could be the case if your genetic data are matched, or if you have a very rare condition. This is a universal issue affecting research and to prevent this, we use appropriate safeguards to protect you.

Will my GP be involved?

Yes, your GP will be notified about your participation in the study. By signing the consent form you are agreeing to this.

What happens if I don't want to carry on with the study?

Your participation is voluntary. If you agree to take part and then change your mind later on, you can withdraw from the study at any point without giving a reason. If you withdraw from the study, it will not affect the standard of care you receive. Your study doctor will discuss alternative treatment with you and offer you the most suitable treatment available.

If you should withdraw fully from the study, study data collected before your withdrawal may still be processed along with other data collected as part of the clinical study. This is so that the overall quality of the study is not impaired. However, no new data will be added to the study database and you may request that all retained identifiable samples are destroyed to prevent future analysis.

What if there is a problem?

Every care will be taken during the course of this study to ensure you receive appropriate care and treatment. If you have any concern about any aspects of the study you should first ask to speak with your study doctor or research nurse, who will try to resolve the problem. If you remain unhappy and wish to complain formally about any aspect of the way you have been approached or treated during the course of this study, you may do so under the standard National Health Service (NHS) complaints procedure, which is available to you at the hospital at which you have received your treatment. We recommend that you obtain a copy of your hospitals complaints procedure or policy if you intend to make a complaint.

[Sites in England] Concerns can also be raised by talking to your local Patient Advice and Liaison Service (PALS). You can contact the PALS team at *[insert Trust name]* on *[insert relevant contact details]*.

[Sites in Scotland] Concerns can also be raised by talking to the Patient Advice and Support Service (PASS). You can contact PASS via the National Citizens Advice Bureau on 0808 800 9060 or through your local Citizens Advice Bureau (www.cas.org.uk/patientadvice).

[Sites in Wales] Concerns can also be raised by talking to the Patient Support and Advisory Service (PSAS). You can contact PSAS on 0300 0200 159 or emailing hdhb.patientsupportservices@wales.nhs.uk.

[Sites in Northern Ireland] Concerns can also be raised by talking to the *[Insert Trust name]* complaints department on *[insert relevant contact details]*.

[Delete above sections as appropriate for location of study site.]

You will be closely monitored both during and after treatment and any side effects will be treated as appropriate. If you suffer any side effects or injury, please notify your study doctor immediately so you can obtain appropriate medical attention.

In the unlikely event that you are injured by taking part, compensation may be available. If you are harmed due to the negligence of someone treating you, then you may have grounds for legal action but you might have to pay for it. NHS Trusts are responsible for clinical negligence and other negligent harm to individuals that are under their care and covered under the NHS Indemnity Scheme.

If you suffer adverse side effects of the study treatment or harm caused by procedures you have undergone specifically for the study you may be able to claim compensation from The Institute of Cancer Research as Sponsor of the HER2-RADiCAL study. In deciding the level of compensation to be awarded, consideration will be given to the likelihood of side effects and any warnings that were given.

What if I have private medical insurance?

If you have private medical insurance please check with the company that your medical insurance policy will not be affected before agreeing to take part in this study.

What will happen to the results of the study?

Independent experts will review the progress of the research, and the results will be published in a scientific journal as soon as there is enough information to be sure the results are reliable. The results will help to decide how to treat HER2-positive breast cancer in the future. The results from this study may also contribute to reviews of worldwide evidence about this type of cancer and its treatment. You will not be identified in any report or publication relating to this research.

The ICR-CTSU's current practice is to provide a summary of any written results provided by the Sponsor or published in a medical or scientific journal to your hospital once available. Your hospital will be able to provide you with a copy of this summary and discuss the results with you further, if you would like.

What if relevant information becomes available?

Sometimes we get new information about the treatment being studied, which may affect your willingness to continue in the study. If this happens, your study doctor will tell you in a timely

manner and discuss whether you should continue in the study. If you decide to continue in the study, you may be asked to sign an updated informed consent form. If you decide to discontinue, your study doctor will make arrangements for your future care.

If the study is stopped for any other reason, we will tell you and arrange your continuing care.

Who has reviewed the study?

The study has been approved by the National Institute for Health Research – Health Technology Assessment (HTA) Programme, Health Research Authority (HRA), the London - South East Research Ethics Committee, the UK Regulatory Agency (MHRA) and the study Sponsor's Committee for Clinical Research. This patient information sheet and consent form has been reviewed by the Patient and Carer Review Panel at The Royal Marsden NHS Foundation Trust and the Independent Cancer Patients' Voice Group.

Additional sources of information and support

You can learn more about research studies and clinical trials on the Cancer Research UK's patient website (www.cancerhelp.org.uk). Macmillan Cancer Support and Breast Cancer Now (https://breastcancernow.org/information-support/support-you/call-our-helpline) are both registered charities providing information, emotional support and publications about all aspects of cancer for cancer patients and their families. You can contact one of Macmillans Cancer Information nurse specialists on the Macmillan Support Line: Freephone 0808 808 00 00 Monday to Friday, 9.00am to 8.00pm. In addition to their nurses, the Macmillan Support Line also has other specialist teams that can provide advice and information relating to welfare benefits, financial issues and everyday practical concerns.

Further reading

You can find more details about the HER2-RADiCAL study on the dedicated webpage located here: 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

The HER2-RADiCAL study has been developed from the findings of previous clinical trials. We have included some examples here in case you wish to learn more about the background to the study. Some of these articles are written in technical language. You do not need to look at these but we are including the links as we know that some people may wish for more information.

Over 4000 patients from across the UK volunteered to take part in a study called PERSEPHONE from 2007 to 2015. This study compared 6 months and 12 months of treatment with trastuzumab in patients with HER2-positive early breast cancer. PERSEPHONE showed that patients treated with 6 months of trastuzumab had no greater risk of the cancer returning than patients treated with 12 months of trastuzumab. The patients treated for 6 months had fewer severe side effects, including heart problems and fewer visits to hospital.

Over the last few years there has been further progress in the way HER2-positive breast cancer is treated and now most patients start their chemotherapy and antibody treatment before surgery. This means that HER2-RADiCAL can use a more personalised approach (by adapting treatment according to the response of the cancer to the treatment before surgery / "pCR") than was possible when the PERSEPHONE study was carried out.

The findings of PERSEPHONE have been published in journals called The Lancet and Health Technology Assessment. You can find a summary of this study at the following location: https://pubmed.ncbi.nlm.nih.gov/32880572/

The idea that patients with a pCR do not need any more chemotherapy after surgery is supported by this research, which found patients with pCR had a high chance of remaining cancer-free whether or not they received more chemotherapy:
https://pubmed.ncbi.nlm.nih.gov/32046998/

The statistics that we quote for the small risk of heart problems and leukemia that can be caused by anthracycline chemotherapy are based on studies such as these:
https://pubmed.ncbi.nlm.nih.gov/29493047/
https://pubmed.ncbi.nlm.nih.gov/15905306/

Thank you for taking the time to consider taking part in this study.

Study contact information

Your doctor for this study is: _____

Your clinical nurse specialist is: _____

Contact phone numbers: _____

The diagrams used within this patient information sheet are based on the PRIMETIME (REC ref no: 16/EE/0305; IRAS no: 190307) patient information diagram, version 1.2, 01 November 2016.

HER2 RADiCAL

To be printed on hospital headed paper

The HER2-RADiCAL study (Response ADaptive CAre pLan) – Tailoring Treatment for HER2-Positive Early Breast Cancer

INFORMED CONSENT FORM
Version 4.0, 01 September 2023

REC Ref: 21/LO/0529 CCR Number: CCR5408 IRAS Project ID: 292122 EudraCT: 2021-001240-10

Centre: Clinician:

Patient's hospital number: Study ID:

Please initial to confirm:

1.	I confirm that I have read and understood the **HER2-RADiCAL PATIENT INFORMATION SHEET, Version 4.0, 01 September 2023** and have had the opportunity to ask questions and had these questions answered satisfactorily.	
2.	I agree to take part and be registered into the HER2-RADiCAL study. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.	
3.	I agree to my initials, full name, date of birth, post code, hospital number and NHS or Community Health Index (CHI) number being sent to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) when I join HER2-RADiCAL.	
4.	I agree to ICR-CTSU using NHS and national health and registration data to keep in touch with me and follow up my health status.	
5.	I understand that sections of my paper and electronic medical records may be accessed and examined by representatives from the ICR-CTSU, the NHS Trust relevant to my taking part in research, the Sponsor (The Institute of Cancer Research), the regulatory authorities and third parties approved by ICR-CTSU to the extent permitted by applicable laws and regulations to make sure the information received is correct. I give permission for these individuals to have access to my records.	
6.	I understand that information collected about me, including genetic details, may be shared within the Sponsor organisation (The Institute of Cancer Research) or with other organisations for the purpose of health and care research which could be outside the UK and the European Economic Area, but that I will not be identifiable from this information.	
7.	I agree to my GP being informed about my participation in this study.	

8.	I agree that tumour tissue and images of tissue samples taken at diagnosis of my breast cancer and during surgery can be used as part of the HER2-RADiCAL study. I understand that my tissue samples may be labelled with my initials, date of birth and unique Study ID number when they are sent to the HER2-RADiCAL central laboratories at the University of Birmingham and The Institute of Cancer Research. I agree for surplus materials and images to be stored indefinitely at the central laboratories or another approved storage facility in the UK.	
9.	I agree that my tumour tissue samples will be analysed for potential changes in DNA (genetic changes). I understand that neither I nor my doctor will be informed of the results of these tests.	
10.	I understand that participation in HER2-RADiCAL involves the completion of patient-reported outcomes questionnaires. I understand that the information I provide on the questionnaires, including my full address, will be sent to the ICR-CTSU.	

OPTIONAL CONSENT

Please initial as appropriate:

		Yes	No
11.	If my cancer comes back, I agree that recurrent tumour tissue collected as part of my standard care can be used as part of the HER2-RADiCAL study. I understand that my tissue samples may be labelled with my initials, date of birth and unique Study ID number when they are sent to the HER2-RADiCAL central laboratories at the University of Birmingham and The Institute of Cancer Research. I agree for surplus materials to be stored indefinitely at the central laboratories or another approved storage facility in the UK.		
12.	I consent to copies of imaging scans (e.g. mammogram, CT, MRI) being used as part of the HER2-RADiCAL study. I understand that I will not be identifiable from these scans.		
13.	If I withdraw from the study, I consent to my doctor providing authorised researchers with basic clinical and other relevant non-clinical information that would be routinely collected and recorded in my medical records.		
14.	I consent to the possible future sharing of information collected about me, including any imaging (relating to my cancer), with other organisations, including those outside of the UK and European Economic Area (EEA) with the understanding that I will not be identifiable from this information.		
15.	I consent to my data, samples and sample images, and copies of scans being stored and used for possible future research, with the understanding that confidentiality will be protected and that ethics committee approval will be obtained before any future research is conducted, if necessary.		

_____	_____	_____
Name of Patient	Signature	Date
_____	_____	_____
Name of Clinician	Signature	Date

Please note, one copy of the patient information sheet and signed consent form should be given to the patient and one copy should be retained in the Site Investigator File