To be printed on hospital headed paper

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IRAS Project ID: 249774

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Sponsor Number: CCR4706

PHOENIX

A trial to look for markers in the tumour cells and blood which signal that trial treatments are working in a patient with triple negative breast cancer, for whom upfront chemotherapy has not provided the maximum expected benefit

PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM FOR TRIAL REGISTRATION

Version: 6.0
Date: 18 Aug 2022

Invitation to take part in a clinical trial

- We are inviting you to take part in a clinical trial called PHOENIX.
- Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve.
- Please take time to read this information sheet carefully and discuss it with friends, relatives and your GP if you wish.
- Ask your trial 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 PHOENIX trial.

Important things to know

- This information sheet provides an outline of the whole PHOENIX trial and describes **Trial Registration** in more detail.
- In this information sheet you will find further details on why we are doing this trial, why you have been invited to participate and what will be involved if you decide to take part.
- By consenting to Trial Registration you are under no obligation to consent to Trial Entry.
- If you would like to see information about Trial Entry now to help make your decision about whether to give consent for Trial Registration, please ask your doctor or nurse for a copy of the PHOENIX Patient Information Sheet for Trial Entry.

ICR The Institute of Cancer Research

CANCER RESEARCH UK

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Why am I being invited to take part in the PHOENIX trial?

You have been invited to participate in this clinical trial, called PHOENIX, because you have been diagnosed with triple negative breast cancer, or TNBC. TNBC is a type of breast cancer in which the cancer cells do not have receptors for the hormones oestrogen and progesterone or for the HER2 protein.

You are in the middle of receiving chemotherapy before having breast cancer surgery. As explained by your doctor, your recent scan or assessment halfway through your chemotherapy has shown that the chemotherapy has not provided you with the maximum expected benefit. This means you may wish to consider finding out if you are eligible for the PHOENIX trial.

Approximately 100 patients from approximately 10 hospitals throughout the UK will be invited to participate in the PHOENIX trial.

Do I have to take part?

No, it is up to you to decide whether or not to take part. Your participation is entirely voluntary and you will be given sufficient time to decide whether or not you wish to participate. Your decision to participate in the trial or not will not affect the standard of care you receive. If you do decide to take part in the trial you are free to withdraw at any time and do not have to give a reason.

What is the purpose of this trial?

We know that in some patients, TNBC can have a high or moderate risk of coming back (or relapsing) after standard treatment. This usually happens within the first two years after finishing standard treatment. We also know that in some patients with TNBC who receive chemotherapy before surgery, if there is cancer remaining after chemotherapy (called residual disease) that risk of relapse is higher.

In PHOENIX we want to look at the biology of the residual disease in the 2-week time window between completing chemotherapy and having surgery. We want to see if taking trial treatment in this window changes the biology of the residual disease. In order to do so we will compare tumour tissue and blood samples collected prior to trial treatment with tumour tissue and blood samples collected after trial treatment but before surgery. If a difference is seen this may be an early sign that the trial treatment could be used to treat this type of cancer in the future and may support further investigation over a longer period of time.

Safety and tolerability of trial treatment will be monitored closely in this trial. Provided it is safe to do so, participants may have the option to receive trial treatment after surgery (called the adjuvant setting) in Part 2 of the PHOENIX trial. The purpose of giving trial treatment in the adjuvant setting is to investigate whether any biological activity is seen within the residual disease after longer exposure to trial treatment over 12 months.

In order for a participant to be suitable to receive trial treatment in Part 2 “circulating tumour DNA” or ctDNA must be present in a blood sample collected 30 days or 3 months after surgery. Looking for the presence of ctDNA in this blood sample is called “ctDNA screening”.

When cells die they release pieces of DNA into the blood stream. The DNA from cancer cells found in the blood is known as ctDNA. It is thought that the presence of ctDNA in the blood can be an early indication that the cancer is at greater risk of relapsing or spreading to another part of the body. Based on previous research, we think that approximately a third of all PHOENIX participants continuing to Part 2 may have ctDNA identified in the ctDNA screening blood sample collected 30 days or 3 months after surgery.

To test for the presence of ctDNA in the blood, a tumour tissue sample needs to be analysed to see if there are particular mutations present that are called "trackable mutations". All participants who are registered to enter the PHOENIX trial will be asked to consent to allow their hospital to provide the biopsy sample stored from when breast cancer was diagnosed. All patients who enter the trial will also be asked to consent to allow their hospital to provide a sample of the tumour from surgery. These samples will be analysed for the presence of trackable mutations.

If trackable mutations are found in the tumour tissue sample, we will invite you to consent for Continuation to Part 2 in order to collect a blood sample for ctDNA screening to look for the same mutations in the blood to confirm the presence or absence of ctDNA. If for any reason trackable mutations cannot be identified in the tumour tissue sample, the participant will not be invited to consent for Continuation to Part 2 because ctDNA screening will not be possible. In this case, the participant's doctor will advise on the treatment options available outside of the PHOENIX trial. Participants may also be offered further treatment outside of the PHOENIX trial after surgery. Depending on the treatment offered, this may also mean that you are not suitable for continuation to Part 2, your doctor will discuss this with you.

What will happen if I decide to take part?

If you agree to take part in this trial you will be given this information sheet to keep and you will be asked to sign a consent form for **PHOENIX Trial Registration**. You will continue to receive chemotherapy as planned, so long as your doctor thinks it is safe for you to do so.

You will need to have some assessments to confirm you are suitable for Trial Registration. Some of these tests are routine, but others will need to be done to make sure that it is safe for you to take part in the trial. These assessments will only be performed after you have agreed to take part by signing a consent form.

The assessments are outlined in the following table:

Assessment	Further details
Review of your medical history and current medication	To check that you are suitable to be registered for PHOENIX.
Physical examination	Including weight, blood pressure, heart rate and temperature.

What if the assessments show that I am not suitable for Trial Registration or I decide that I do not want to take part?

If the assessments show that you are not suitable for Trial Registration or you decide you do not want to participate in this trial your doctor will discuss the treatment options available outside of this trial with you.

What happens next if I am suitable for Trial Registration?

If after the assessments have been performed your doctor confirms that you are suitable for Trial Registration, you will be registered into PHOENIX.

After registration a scan will be performed at least 1 week after day 1 of your final cycle of neoadjuvant chemotherapy to confirm whether there is breast cancer tissue remaining and that you may be suitable for Trial Entry.

If you have to stop chemotherapy earlier than planned due to side effects after Trial Registration, you may still be able to take part in PHOENIX Trial Entry providing you have recovered from the side effects of chemotherapy and the assessments show you are suitable for Trial Entry in every other way.

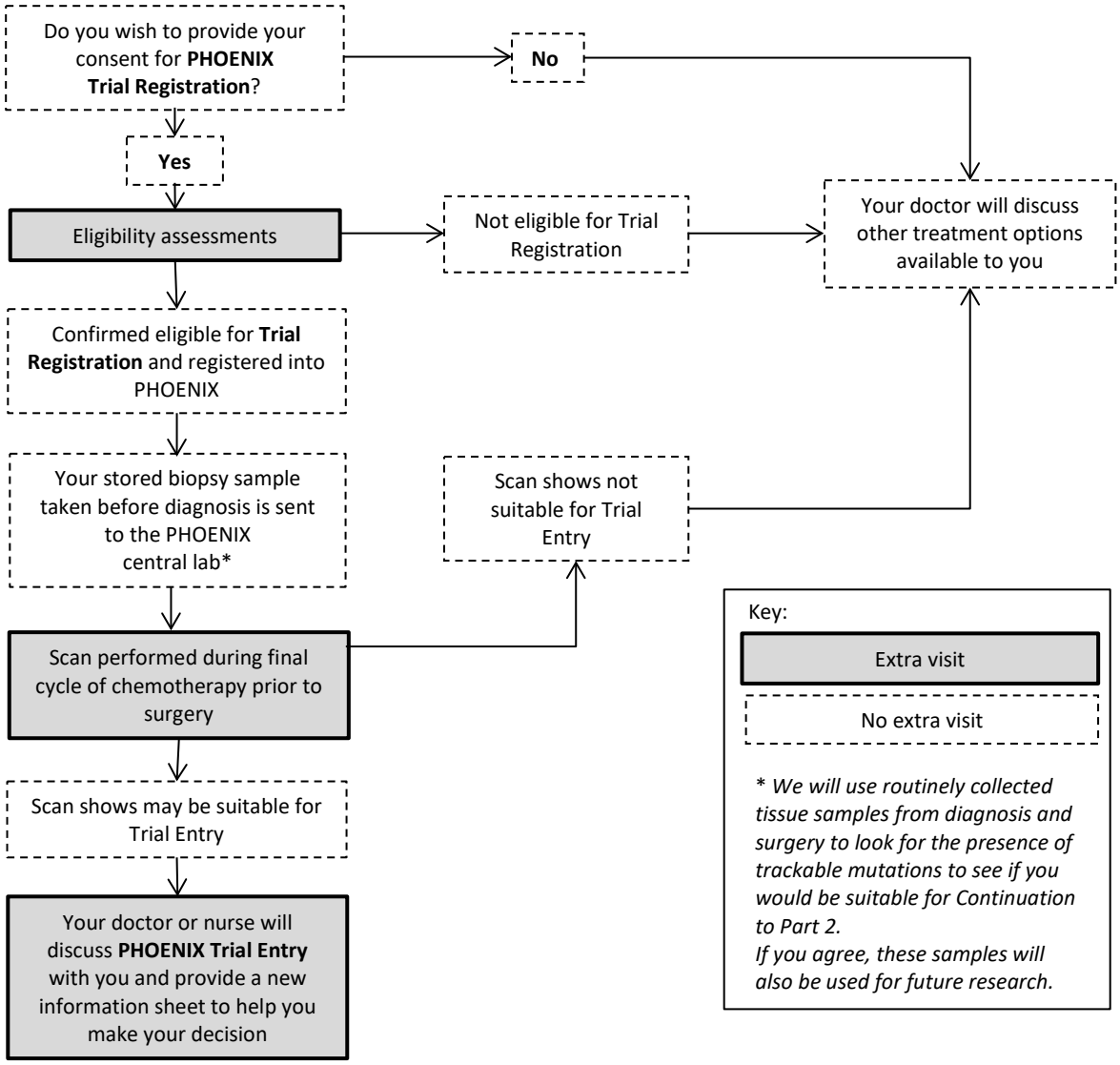
If the scan shows that you are not suitable for Trial Entry or you decide you do not want to participate in PHOENIX any more, your doctor will discuss the treatment options available outside of this trial with you.

You will be asked to consent to allow your hospital to provide the biopsy sample they have stored from when breast cancer was diagnosed. We would like to use this for future cancer research. If you are found to be suitable for trial entry after your scan, we would also like to use this sample to look for the presence of trackable mutations. This will determine whether you could be suitable for Continuation to Part 2 of the PHOENIX trial. If you are found to be suitable for trial entry, and later for continuation to Part 2, you will be given more information on this in separate information sheets.
If the scan shows that you may be suitable for Trial Entry, you will be given another information sheet explaining what is involved in **PHOENIX Trial Entry**. This information sheet will describe the assessments you will be asked to have, including biopsies and blood samples, and more detail about the trial treatments, including side effects in order for you to decide if you would like to consent for Trial Entry. If you would like to see this information now to help make your decision about whether to give consent for Trial Registration, please ask your doctor or nurse for a copy of the PHOENIX Patient Information Sheet for Trial Entry.

By consenting to Trial Registration within PHOENIX you are under no obligation to consent to Trial Entry. You can change your mind and are free to withdraw from any part of this trial at any time if you want to.

The following flow chart clearly sets out the steps involved in taking part in PHOENIX Trial Registration. A few steps involve an extra visit to the hospital.

PHOENIX Flow Chart: Trial Registration



What are the possible benefits of taking part in the PHOENIX trial?

It is important to understand that you may not get any direct benefit from participating in PHOENIX. However, your participation is likely to help us identify whether any of the trial treatments could be an effective therapy for patients with TNBC in the future. We hope that the trial will help to select those treatments which should be further investigated in a larger clinical trial to see if they are better than currently offered treatments, and find answers to questions that could help to improve the treatment for future patients with TNBC.

What are the possible disadvantages and risks of registering for PHOENIX?

The disadvantages and risks of registering for PHOENIX are detailed below:

i. Additional hospital visits

Registering for this trial may involve several additional visits to the clinic. This may cause some disruption to your normal activities and home life and this should be discussed with your family

and friends if it will impact on them. We will be able to reimburse you for any extra travel expenses; your doctor will discuss this with you.

ii. Scan to confirm residual disease

A scan would typically be performed following neoadjuvant chemotherapy as part of your routine care. If you register for PHOENIX the information from a scan, performed at least 1 week after day 1 of your final cycle of neoadjuvant chemotherapy, will be used to determine if you may be suitable for Trial Entry. In most cases the type of scan you will have will be an MRI scan, but in some cases an ultrasound scan or tomosynthesis mammography may be performed. MRI scans use magnetic and radio waves to take pictures of the inside of your body. Although there is no x-ray exposure with an MRI, the procedure takes longer (40 minutes to an hour) and involves keeping still while lying down on the scanner table. It can be noisy and you will be in a narrower tunnel compared to CT scan. Some patients may feel claustrophobic and may experience discomfort related to lying still in an enclosed space for a prolonged period of time while the MRI scan is being taken. Your local hospital team should be able to offer support to help you feel more comfortable during the scan. Tomosynthesis mammography uses x-rays to form images of your body. X-rays are a type of ionising radiation which may cause cancer many years or decades after the exposure. The chances of this happening to you as a consequence of taking part in this study are about 0.02%.

iii. Private medical insurance

If you have private medical insurance you should check with the insurance company before agreeing to take part in this trial to ensure that your participation will not affect your cover.

What will happen to my tissue sample?

When you are registered for the PHOENIX trial we ask all participants to allow their hospital to provide the biopsy sample they have stored from when breast cancer was diagnosed.

Any samples you donate will be used to help us understand how cancer reacts to trial treatment.

The tissue sample that you donate will be sent to the trial central laboratory at the Institute of Cancer Research and Royal Marsden NHS Foundation Trust where it will be securely stored.

Your sample will be labelled with your initials, date of birth, date of sample collection and unique Trial Registration Number when it is sent to the central laboratory so we can identify each sample. When it arrives at the trial central laboratory, a unique laboratory code will be allocated to each sample. The coding will maintain your confidentiality whilst allowing biological details to be compared to clinical findings.

In addition, we would like to use your tissue for further research within the PHOENIX trial. For such research it may be necessary to use commercial companies to carry out tests on the sample. For example, in situations where the research organisations do not have access to specialist equipment and/or where using a commercial company may be more cost-effective because they can carry out a greater volume of tests within a short time frame. In such cases, after testing is complete the commercial company would return all result data and any surplus samples to the research organisation and would not be permitted to use the data or samples for their own research.

In order to gather more information, we may share your samples and/or information we gain from your samples, including genetic details, with other cancer researchers at other specialist research

laboratories in the UK, the EU or outside the EU. Your samples and information about your cancer will be anonymised before they are shared meaning you cannot be identified from the sample/information. This will not affect your care or influence whether or not you receive PHOENIX trial treatment.

If you give your permission, after the PHOENIX trial is complete, any leftover samples will be stored at the trial central laboratory for use in future medical research that may involve research by other health and research organisations.

Any research using your samples will have approval from a Research Ethics Committee and you will not be identifiable from the sample. If any future research undertaken leads to a new treatment or test that becomes commercially viable, you will not financially benefit from this.

How will confidentiality be maintained?

The Institute of Cancer Research is the sponsor for this trial based in the United Kingdom. We will be using information from you and your medical records in order to undertake this trial and will act as the data controller for this trial. 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 trial 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. The procedures for handling, processing, storage and destruction of your data will be compliant with the Data Protection Act 2018 and in accordance with the UK Policy Framework for Health and Social Care Research.

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 trial, 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 or your rights:

- at https://www.icr.ac.uk/legal/privacy
- by sending an email to ICR's Data Protection Officer at dataprotectionofficer@icr.ac.uk
- at www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/transparency
- at www.hra.nhs.uk/information-about-patients

[Insert appropriate name for NHS site] will collect information from you and your medical records for this research trial 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 trial, and make sure that relevant information about the trial is recorded for your care, and to oversee the quality of the trial.

All information which is collected about you during the trial will be kept strictly confidential. When you register for the trial, your initials and date of birth will be passed to The Institute of Cancer Research

Clinical Trials and Statistics Unit (ICR-CTSU) where the trial is being coordinated. You will be given a unique Trial Registration 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 working on PHOENIX will have access to the information that could allow this Trial Registration Number to be linked to you.

Representatives from the ICR-CTSU, the NHS Trust relevant to your taking part in research, the Medicines and Healthcare products Regulatory Agency (MHRA) and ethics committee approving the trial, the pharmaceutical company, AstraZeneca which manufactures the trial drug and may have offices outside of the UK/EU and third parties approved by ICR-CTSU may need to examine your medical records to the extent permitted by applicable laws and regulations to make sure the information received is correct. All information will be kept confidential.

The information collected will be kept by the ICR for at least 5 years and *[Insert appropriate name for NHS site]* will keep identifiable information about you from this trial for at least 5 years after the trial has finished.

Data sharing

When you agree to take part in a research trial, 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 United Kingdom General Data Protection Regulation (UKGPR) or how we use your information please contact our Data Protection Officer at dataprotectionofficer@icr.ac.uk.

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

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

If you should withdraw fully from the trial, no new data will be added to the trial database however trial data collected before your withdrawal may still be processed along with other data collected as part of the clinical trial. This is so that the overall quality of the trial is not impaired.

What if there is a problem?

If you have any concern about any aspects of the trial you should first ask to speak with your trial 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 trial, you may do so under the standard National Health Service (NHS) complaints procedure, which is available to you at your doctor's hospital. 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 0808800 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.
[*Delete above sections as appropriate for location of trial site.*]

You will be closely monitored both during and after trial treatment and any side effects will be treated as appropriate. If you suffer any side effects or injury, please notify the trial 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 trial treatment or harm caused by procedures you have undergone specifically for the trial you may be able to claim compensation from The Institute of Cancer Research as Sponsor of the PHOENIX trial. 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 trial.

Who is funding and organising the trial?

The trial is funded by AstraZeneca, the pharmaceutical company who manufacture the trial treatments (AZD6738, olaparib and durvalumab). AstraZeneca are supplying the trial treatments free of charge and providing additional funding to support the management of the trial.

The trial is organised by the Institute of Cancer Research (led by Professor Andrew Tutt). The trial is coordinated by The Institute of Cancer Research Clinical Trials & Statistics Unit (ICR-CTSU). The trial is being carried out by a network of doctors across the UK. The trial funding helps to cover the cost of including information about you in the trial, the laboratory tests and helps support the research staff. None of the researchers are personally benefiting from this funding.

Who has reviewed the trial?

Cancer Research UK has reviewed PHOENIX and supports the aims of the trial. PHOENIX has also been approved by the UK Regulatory Agency (Medicines and Healthcare Regulatory Agency, MHRA), a Research Ethics Committee (London - South East Research Ethics Committee) and the Health Research

Authority (HRA). Their approval means they are satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits, and that you have been given the right information to decide whether to take part.

What will happen to the results of the trial?

Independent experts will review the progress of the trial, and the results will be published in a scientific journal as soon as there is enough information to be sure the results are reliable. Once available, the results will also be available on the Cancer Research UK trials database (https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial).

The results will help to decide which trial treatments we should look at more closely in a bigger clinical trial and how to treat patients with TNBC in the future. The results from this trial 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.

What happens now?

Your doctor or nurse will be happy to answer any questions. Once you have reached your decision please let your doctor or nurse know. If you choose to consent to PHOENIX Trial Registration you will be asked to sign a consent form and will be given a copy to keep together with this information sheet.

Further information

Macmillan Cancer Support is a registered charity providing information, emotional support and publications about all aspects of cancer for cancer patients and their families.
You can contact one of their 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.

You can learn more about clinical trials and the results of this trial once available on the Cancer Research UK's patient website (**http://www.cancerresearchuk.org/cancer-help/trials/**).

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

Your specialist is: _____

Contact phone numbers: _____

To be printed on hospital headed paper

INFORMED CONSENT FORM FOR TRIAL REGISTRATION

Version 6.0, 18 Aug 2022

REC Ref.: 19/LO/0127
IRAS Project ID: 249774

EudraCT: 2018-002077-21
Sponsor Number: CCR4706

Centre: _____ Clinician: _____

Patient's hospital number: _____ Registration Number: _____

Please initial

1. I confirm that I have read and understood the **PHOENIX PATIENT INFORMATION SHEET FOR TRIAL REGISTRATION, Version 6.0, dated 18 Aug 2022** and have had the opportunity to ask questions and had these answered satisfactorily. ☐
2. I agree to take part and be **registered into the PHOENIX Trial**. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I agree to my initials and date of birth being sent to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) when I register for the PHOENIX Trial. ☐
4. I understand that sections of my medical records may be 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 ethics committee approving the trial, AstraZeneca (the pharmaceutical company that manufacture and supply the trial treatment) 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. ☐

Patient's hospital number: _____ Registration Number: _____

Please initial

5. 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, but that I will not be identifiable from this information. ☐

6. I agree that tumour tissue taken from my breast cancer at diagnosis can be used as part of this trial and sent to specialist research laboratories in the UK for analysis. ☐

7. I consent to my tumour tissue samples from my breast cancer at diagnosis being stored for possible future medical research, with the understanding that confidentiality will be protected and that Research Ethics Committee approval will be obtained before any future research is conducted. ***(Optional – please initial Yes or No)***

Yes ☐ No ☐

Name of Patient	Signature	Date
Name of Researcher	Signature	Date