To be printed on hospital headed paper

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

EudraCT: 2018-002077-21
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 ENTRY

Version: V6.0
Date: 27 Oct 2022

Invitation for PHOENIX clinical Trial Entry

- You have been given this patient information sheet because you previously registered for the PHOENIX clinical trial and we are now inviting you to proceed to Trial Entry.
- Before you decide whether to participate further, 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 proceed to **PHOENIX Trial Entry**.

Important things to know

- This information sheet provides information you will need to know to make an informed decision about whether to proceed to Trial Entry.
- In this information sheet you will find further details on why we are doing this trial, why you have been invited to proceed to Trial Entry and what will be involved if you decide to participate further.
- The three appendices at the back of this information sheet provide further information on the trial treatments being investigated. It is up to you whether you read all of the appendices up front, or whether you wait until after you have entered the trial and read the information on the specific trial treatment you are allocated to.
- There is a separate information sheet to describe Continuation to PART 2 of the trial. You will be given this futher information sheet if you are suitable to consider taking part further after your planned surgery.
- By consenting to Trial Entry you are under no obligation to consent for Continuation to PART 2.

ICR The Institute of Cancer Research

CANCER RESEARCH UK

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Why am I being invited to enter the PHOENIX trial?

You have been given this information sheet because you previously agreed to register for the PHOENIX trial. You had a scan for the trial during your final cycle of chemotherapy, which showed that there is breast cancer tumour remaining, meaning you may be suitable to proceed to PHOENIX Trial Entry. This may involve receiving a trial treatment for two weeks before your planned surgery.

Do I have to take part?

No, it is up to you to decide whether or not to proceed to PHOENIX Trial Entry. 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.

A reminder of the purpose of PHOENIX

We know that in some patients, triple-negative breast cancer (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 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 either 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 fifth of all PHOENIX participants continuing to Part 2 may have ctDNA identified in the ctDNA screening blood sample collected at 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 for the PHOENIX trial were asked to consent to allow their hospital to provide the biopsy sample stored from when breast cancer was diagnosed and you will now be asked to consent to allow

your 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 the participant 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 proceed to Trial Entry you will be given this information sheet to keep and you will be asked to sign a consent form for **PHOENIX Trial Entry**.

You will need to have some assessments before you can proceed to Trial Entry. These tests are done to make sure that you are suitable to proceed to Trial Entry and that it is safe for you to receive trial treatment. These assessments will only be performed after you have agreed to proceed to Trial Entry by signing a consent form. They may all be done together during one visit, or across a few different visits. Your doctor will talk to you about this.

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 proceed to Trial Entry.
Physical examination	Including height, weight, blood pressure, heart rate and temperature.
Collection of blood samples for routine tests	Approximately 4 teaspoons (20ml) of blood will be taken for routine safety checks to confirm you would be suitable to receive trial treatment if allocated.
An electrocardiogram (ECG)	To assess your heartbeat rhythm.
A pregnancy test	A pregnancy test will be carried out for all women who are able to get pregnant.

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

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

What happens next if I am suitable for PHOENIX Trial Entry?

If after the assessments your doctor confirms that you are suitable for Trial Entry we will randomly allocate you to one of four groups or 'cohorts'.

It is important that the participants in the four cohorts are as similar to each other as possible. This is because we need to be sure that if one cohort fares better than the other cohorts, it is because of the trial treatment and not because the participants in the cohorts are different from each other in some way. A computer programme is used to perform the random allocation to make sure this is done fairly.

You will be told by your trial doctor or nurse which cohort you have been allocated to.

The four cohorts are as follows:

Cohort	What will I be given?		How it will be given?
A	Standard care	Participants in this cohort will not receive any trial treatment between the end of chemotherapy and breast cancer surgery. This cohort is important as it helps us to work out whether any changes we see in cohorts B, C or D are due to the trial treatment.	No trial treatment given
B	AZD6738	AZD6738 belongs to a group of drugs known as ATR inhibitors. They are involved in sensing DNA damage and stopping the cancer cell dividing.	Tablets taken twice daily for 10 days
C	Olaparib	Olaparib belongs to a group of drugs known as PARP inhibitors. Blocking PARP with olaparib may prevent the cancer cells from repairing their DNA causing them to die.	Tablets taken twice daily for 14 days
D	Durvalumab	Durvalumab is a type of immunotherapy. Sometimes the body's own immune system may slow down or control cancer growth. Sometimes though, this natural immune system response stops, and the cancer is not killed by the body's own immune system. Research has shown that in some participants, cancer cells and immune cells start to give signals that stop the body's immune system from killing the cancer. New drugs like durvalumab work to block this signal and to increase the immune response. It is hoped that by blocking this signal, the immune cells within the participants's body will once again be able to prevent or slow down cancer growth.	Infusion, on day 1 only

If you are allocated to a treatment cohort you will be given a prescription for the trial treatment and be instructed on how to take it.

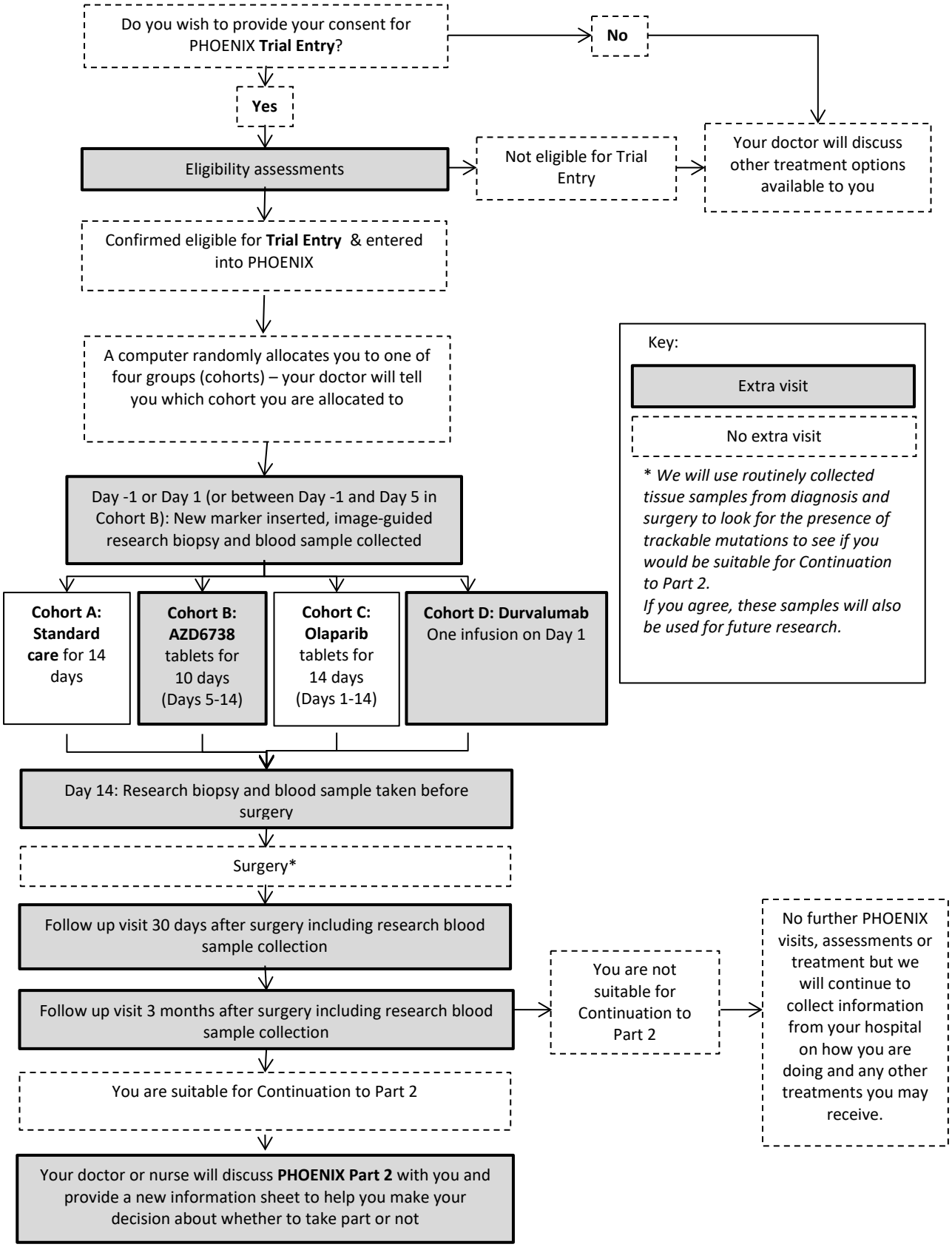
Up to 24 patients will be randomly allocated to each of the treatment cohorts. Once 9 patients have received treatment in each cohort the results of how each patient responded to treatment will be evaluated. If no changes are observed with a particular treatment then that cohort will be closed and no further patients will be allocated to receive that trial treatment.

The three appendices at the back of this information sheet provide further information on the trial treatments being investigated. This includes information on the treatment dose, administration, duration, potential side effects and what other medications should be avoided while taking the treatment. It is up to you whether you read all of the appendices up front, or whether you wait until after you have entered the trial and read the information on the specific trial treatment you are allocated to.

At trial registration you were asked to consent to allow your hospital to provide the biopsy sample they have stored from when breast cancer was diagnosed and will now be asked to consent to allow your hospital to provide a sample of the tumour from your surgery. We would like to use this for future cancer research. We would also like to use this sample to look for the presence of trackable mutations to see if you would be suitable for Continuation to Part 2 of the PHOENIX trial. If you are found to be suitable to continue to Part 2 you will be given more information on this in a separate information sheet after your planned surgery in order to consider whether you would like to continue to participate in PHOENIX further.

The following flow chart sets out the steps involved in PHOENIX Trial Entry. Some steps will involve an extra visit to the hospital.

PHOENIX Flow Chart – Trial Entry



What assessments will be performed if I proceed to Trial Entry?

You will see one of the trial doctors at regular clinic visits to monitor your progress. These visits will take place at:

- On Day -1 or Day 1 (or Day -1 to Day 5 if you are allocated to Cohort B) of the 2-week window
- Day 14, up to 3 days before your planned surgery
- 30 days after surgery
- 3 months after surgery

If you are taking a trial treatment, the trial doctor will also monitor any side effects during these visits.

During the clinic visits you will also have regular assessments, two biopsies and three blood sample collected, as outlined in the following tables:

Timing of assessments in clinic	
Assessment	**Timing of assessment**
Discussion with your trial doctor to document changes in your health or medications since your last visit	• Day -1 or Day 1 (or Day -1 to Day 5 for Cohort B) • Day 14 • 30 days after surgery • 3 months after surgery
Physical examination including measurements of your weight, blood pressure, heart rate and temperature	• Day -1 or Day 1 (or Day -1 to Day 5 for Cohort B) • Day 14 • 30 days after surgery • 3 months after surgery
An electrocardiogram (ECG), to assess your heartbeat rhythm	• Day -1 or Day 1 (or Day -1 to Day 5 for Cohort B) • 30 days after surgery • 3 months after surgery
Cohorts B and C only: Review of your completed patient diary card for 2 week window of treatment	• Day 14
Discussion with you trial doctor regarding whether you are suitable for Continuation to Part 2. If your doctor confirms you are suitable for continuation you will be given further information on PHOENIX Part 2 at this visit.	• 30 days after surgery and/or • 3 months after surgery
Pregnancy test for all participants who are able to get pregnant	• Day 1 for Cohort C only • 30 days after surgery

Timing of research biopsies	
Type of biopsy	**Timing of collection**
Baseline image-guided biopsy, guided by a new marker insertion	Day -1 or Day 1 (or Day -1 to Day 5 for Cohort B)

Timing of research biopsies	
Pre-surgery image-guided biopsy, guided by the marker inserted at the start of the window	Day 14

Timing of blood sample collections in clinic		
Type of blood sample	**Amount of blood that will be taken**	**Timing of collection**
Blood tests for routine safety checks	15ml (3 teaspoons)	• Day -1 or Day 1 (or Day -1 to Day 5 Cohort B) • Day 14 • 30 days after surgery • 3 months after surgery
Research blood sample to explore biomarkers which may help to predict how well treatment will work for individuals	Up to 40ml (8 teaspoons)	• Day -1 or Day 1 (or Day -1 to Day 5 Cohort B) • Day 14 • 30 days after surgery
Research blood sample to explore biomarkers which may help to predict how well treatment will work for individuals	Up to 30ml (6 teaspoons)	• 3 months after surgery if required
All cohorts at selected hospitals only: Research blood sample for assessment of your immune system's recognition of mutations present in your cancer	20ml (4 teaspoons)	• Day -1 or Day 1 • Day 14 • 30 days after surgery
Research blood samples taken on Day 1 (or Day 5 for Cohort B) will need to be taken before the start of trial treatment; if you are in Cohort B or C you should wait to start your tablets until after your blood samples have been collected.		
Research blood samples taken on Day 14 will need to be taken after your final dose of trial treatment; if you are in Cohort B or C you should make sure you have taken your final tablets before your blood samples have been collected.		
The maximum amount of blood that will be collected for research purposes at any clinic visit is 105ml (less than 21 teaspoons).		

You need to consider carefully how these assessments and hospital visits will affect you and your family. Please ask your doctor or nurse if you have any questions about the tests and procedures.

What are the side effects of trial treatment?

As with any drug, AZD6738, olaparib and durvalumab can have side effects. No-one can predict before you begin trial treatment whether you will have any of these, or how serious they might be. Further information on the trial treatments and potential side effects of each are described in the appendices of this information sheet. It is up to you whether you read all of the appendices up front, or whether you wait until after you have entered the trial and read the information on the specific trial treatment

you are allocated to. Not all participants will experience these side effects and medications can be given to make any side effects less serious or less uncomfortable.

All drugs have the potential risk of an allergic reaction which if not treated promptly could become life threatening. **You should seek medical advice and contact your trial doctor or research nurse immediately if you have trouble breathing or have swelling of the face, mouth, lips, gums, tongue or neck.**

It is important that you report all symptoms and side effects that you may experience to your trial doctor or research nurse as soon as they occur, whether or not you think they are caused by the trial treatment so they can advise you what to do.

Can I take other medication whilst participating in PHOENIX?

As with any drug when taking AZD6738, olaparib or durvalumab you may have avoid other medications. Further information on the trial treatments including any specific instructions whilst taking trial treatment are described in the appendices of this information sheet. It is up to you whether you read all of the appendices up front, or whether you wait until after you have entered the trial and read the information on the specific trial treatment you are allocated to.

Will there be anything extra I need to do if I take part in the treatment cohort?

If you decide to take part, you will need to:

- Sign the consent form for Trial Entry to show you understand what participation involves.
- Attend all scheduled appointments.
- Take your trial treatment as directed.
- Only take the trial treatment yourself.
- Store any medication provided to you in the bottle given to you by your trial doctor or pharmacist as directed on the label (Cohorts B and C only).
- Keep your treatment out of the reach of children.
- Talk to your trial doctor or research nurse first if you want to stop taking the trial treatment for any reason.
- Report all symptoms and side effects that you may experience to your trial doctor or research nurse as soon as they occur, whether or not you think they are caused by the trial treatment.
- Tell your doctor about any other medicines that you take, even if you buy them without a prescription; this includes over the counter medications or herbal supplements.
- Tell your doctor about any medical problems you have.
- Return any medicine containers (with any leftover tablets) to the trial team at each visit (Cohorts B and C only).

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

It is important to note 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 effective for the treatment of TNBC. 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 the treatments currently offered, 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 taking part in PHOENIX?

The disadvantages and risks of taking part are detailed below:

i. Additional hospital visits

Taking part in this trial will 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. Blood tests

As shown in the flow chart on page 8 of this information sheet, taking part in the PHOENIX trial requires you to give several blood samples. The number of blood samples required in this trial is more than if you were receiving standard care outside of this research trial. Risks linked with collecting blood samples from your arm include pain from the needle being inserted, bruising, light-headedness, possible fainting and (rarely) infection.

iii. Biopsies

As shown in the flow chart on page 8 of this information sheet, taking part in the PHOENIX trial requires you to give two extra tissue biopsies. The number of biopsies required in this trial is more than if you were receiving standard care outside of this research trial.

The local anaesthetic you receive before the biopsy procedures will be injected using a syringe and a small needle and may cause a brief stinging sensation. If you have any known allergies relating to anaesthetics these should be discussed with your study doctor. The taking of a biopsy may cause some pain, redness, swelling, slight bruising at the biopsy site and rarely fainting. There is a small risk of bleeding, infection, wound healing problems following your biopsy. You will have the opportunity to discuss all the possible side effects and the type of biopsy with your study doctor.

iv. Electrocardiogram

The electrocardiogram for the electrical tracing of your heartbeat involves placing small electrodes on the surface of your skin. Rarely, a slight redness or inflammation may appear due to the adhesives used to attach the electrodes to the skin.

v. Side effects of trial treatment:

AZD6738 and durvalumab are both unlicensed drugs, which means that they are regarded as experimental and not all of their side effects are yet known. Olaparib is a licensed drug which is in use in several types of cancer, however in this trial we are treating some participants who would not normally receive this drug, which means that it is also regarded as experimental and not all of its side effects are yet known. You may therefore experience some side effects that are not anticipated and are not listed in the previous sections. There is no way of predicting if you will experience any side effects, or how severe they will be. You should contact your trial doctor if you experience any side effects, even if you are not sure that any problems you may have are related to taking the trial treatment. Occasionally some participants need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious.

vi. Radiation exposure

By participating in PHOENIX you may have up to two image guided breast biopsies. You would probably not have these procedures if you did not take part in the study. Biopsies will typically be collected using ultrasound imaging but in some cases stereotactic or tomosynthesis mammography may be used which involve x-rays. Stereotactic and tomosynthesis mammography involve small exposures to ionising radiation. Ionising radiation can have an adverse effect on the body, including

a small increased risk of causing a cancer several years after the exposure. However, the chance of this happening to you as a consequence of taking part in this study is extremely small. There is no radiation dose burden associated with ultrasound imaging.

vii. Risks to an unborn child

There could be risks to an unborn child if you commence trial treatment; therefore, if you are pregnant you cannot enter the trial. If you become pregnant during the trial, these risks could affect you or your unborn child. Before commencing trial treatment, during trial treatment and at the end of trial treatment, pregnancy tests will be carried out for all women who are able to get pregnant. If applicable, you must agree to practice total abstinence or to use a condom and one highly effective form of contraception in combination (as listed below) during trial treatment and for a period of at least 6 months after the last dose of trial treatment.

Highly effective birth control methods used must include ONE of:

- Vasectomised sexual partner. With assurance that the vasectomised partner has received post-vasectomy medical confirmation of surgical success (azoospermia).
- Bilateral tubal occlusion.
- Intrauterine device (IUD), provided coils are copper-banded.
- Combined (estrogen and progestogen containing) oral hormonal contraception pill associated with inhibition of ovulation.
- Cerazette (desogestrel).
- Hormonal injection (e.g. Depo-Provera).
- Etonogestrel implants (e.g. Implanon, Norplant).
- Norelgestromin / ethinyl estradiol (EE) transdermal system.
- Intrauterine system (IUS) device (e.g. levonorgestrel releasing IUS - Mirena®).
- Intravaginal device (e.g. EE and etonogestrel).

If you think you may be pregnant, you must tell your trial doctor immediately. Pregnancy will be a reason to stop trial treatment. If you become pregnant, information on the outcome of your pregnancy will be requested.

viii. 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 does having a biopsy involve?

A biopsy is the removal of a small piece of tissue from the tumour. All biopsies in PHOENIX will be taken using a biopsy needle through the skin, and should take about 15-30 minutes to do. The doctor will try to collect up to 8 samples each time a biopsy is performed.

During the baseline biopsy at the start of the 2-week window before surgery, the doctor will insert a very small marker (sometimes referred to as a “coil”) into the part of the tumour that they are

interested in, so that all biopsies collected for PHOENIX are taken from the same location. This is important as it means we will be comparing the same part of the tumour at the start and end of the 2-week window.

The doctor taking the biopsy will use imaging to see where the tumour is. In the majority of cases ultrasound imaging will be used but in some cases x-ray based techniques may be used. The marker will show up on the scan to guide the doctor to the right part of the tumour. You will have a local anaesthetic first to numb the area. It may still be painful or a little uncomfortable afterwards, but mild painkillers such as ibuprofen should help. There may be a small amount of bleeding, which is normal, and your doctor or nurse will make sure this has stopped before you go home.

Your doctor or nurse will give you information about how to care for the biopsy wound. Very few biopsies start to bleed again. If this does happen, press on the area with a clean cloth. This will help your blood to clot and the bleeding to stop. If it does not stop please contact your doctor. Some wounds may require some stitches, which will need to be removed after a few days; your doctor or nurse will give you information about how to arrange this.

A biopsy is an invasive procedure and there is a very small risk of perforation of a blood vessel and a risk of infection. These complications may be life threatening but the risk is less than 1 in 10,000.

What will happen to my tissue and blood samples?

In 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, a sample of the tumour from your surgery and any samples taken as part of your routine care if your cancer comes back once you have finished trial treatment but while you are still being followed up for the trial. Additionally, you will be asked to have new tumour tissue biopsies and blood sample collections for research into your tumour during the trial. Details of the samples requested throughout PHOENIX are described on page 10 of this information sheet.

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

Tissue and blood samples that you donate throughout the PHOENIX trial (upon Trial Registration, Trial Entry and Continuation to Part 2 and during follow-up) will be sent to the trial central laboratory at the Institute of Cancer Research and Royal Marsden NHS Foundation Trust where they will be securely stored.

All your samples will be labelled with your initials, date of birth, date of sample collection and unique Trial ID Number when they are sent to the central laboratory so we can identify each sample. When they arrive 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.

Some of your tissue and blood samples will stay at The Institute of Cancer Research and Royal Marsden NHS Foundation Trust for laboratory researchers to look at to see what the PHOENIX trial has found.

In addition, we would like to use your tissue and/or blood samples for further research within the PHOENIX trial. For such research it may be necessary to use commercial companies to carry out tests on the samples. 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 enter 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 trial 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 working on PHOENIX 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, ICR-CTSU 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 out how you are. 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 full 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 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 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 UK General Data Protection Regulation (UKGDPR) or how we

use your information please contact our Data Protection Officer at dataprotectionofficer@icr.ac.uk.

Involvement of your General Practitioner (GP)/family doctor

Your GP will be informed about your participation in the PHOENIX trial if you decide to enter the trial and the specific cohort you have been allocated to. This will ensure that your GP knows if you are taking trial treatment in the event of any potential side effects and/or drug interactions.

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 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 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, trial data collected before your withdrawal may still be processed along with other data collected as part of the clinical trial. However you may request that all retained identifiable samples are destroyed to prevent future analysis.

You will be asked to return to the clinic to undergo the tests and evaluations scheduled for the safety follow-up visit. You retain the right to decide whether data from the visit can be used.

If you were to withdraw from the trial, we would like your permission for your hospital to continue to send basic clinical information on your progress that would routinely be collected and written in your medical records to ICR-CTSU. This is so that the overall quality of the trial is not impaired. Please initial the consent form to confirm your permission for this.

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 treatment 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 if relevant new information becomes available?

Sometimes during the course of a trial, new information becomes available about the trial treatments being studied. If this happens, your trial doctor will tell you about it and discuss whether you want to, or should, continue in the trial. If you decide not to carry on, your doctor will make arrangements for your continued care. If you decide to continue in the trial you may be provided with an updated information sheet and asked to sign an updated consent form.

If the new information means it would be in your best interests to withdraw you from the trial, your doctor will explain the reasons for this and arrange for your continued care. If the trial is stopped for any other reason, you will be told why and your doctor will arrange for your continued care.

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 continue to PHOENIX Trial Entry 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 continuing to participate in this trial.

Your specialist is: _____
Contact phone numbers: _____

Appendix for Cohort B: AZD6738 treatment for 10 days before surgery

Important things to know

This appendix contains detailed information on the trial treatment **AZD6738** including information on the possible side effects and any specific instructions you will need to follow when receiving trial treatment.

What is AZD6738?

AZD6738 belongs to a group of drugs known as ATR inhibitors. They are involved in sensing DNA damage and stopping the cancer cell dividing. It is thought that AZD6738 may be an effective treatment option for patients with TNBC.

How should AZD6738 be taken?

The treatment is administered during the 2-week window between finishing chemotherapy and before surgery. In this short period of time you will take AZD6738 for 10 days starting from Day 5 of the 2-week time period to Day 14. At the start of trial treatment you will be given a sufficient supply of AZD6738 tablets for 10 days to take home with you. AZD6738 tablets should be taken orally twice a day. You should not eat any food for 2 hours before and 1 hour after taking your tablets. Drinking water in those 2 hours is ok. The tablets should be taken whole and should not be split, chewed, crushed or dissolved.

You will need to take a total dose of 320mg per day (160 mg twice a day). This should be taken as two separate 160mg doses taken approximately 12 hours apart at the same times each day, or as directed by your trial doctor or research nurse. You will need to do this every day for 10 days (Day 5 to Day 14) from the start date as directed by your trial doctor or research nurse.

You may take your AZD6738 tablets up to 2 hours after the scheduled dose time. If you forget to take a dose of AZD6738 and if more than 2 hours has passed since your scheduled dose time or you are sick shortly after taking a dose of AZD6738 you should continue to take the next dose as scheduled. You should not take extra tablets to make up a missed dose.

Please store your AZD6738 tablets at room temperature and out of direct sunlight. There may be some tablets left in the bottle at the end of the 10 days of treatment, and you should bring the bottle containing the leftover tablets to the clinic visit after completing trial treatment.

How long will I receive AZD6738 for?

You will receive trial treatment for 10 days (Day 5 to Day 14) in the 2-week window after completing your chemotherapy and before surgery, unless you need to stop due to side effects of the treatment.

After surgery your doctor will discuss with you what your next options for treatment are.

What are the side effects of treatment with AZD6738?

As with any treatment, AZD6738 can have side effects. No-one can predict before you begin treatment whether you will have any of these, or how serious they might be. AZD6738 is an experimental drug without a license and therefore the frequency of some of the listed side-effects is not certain. Side effects that have been previously reported are listed below. Not all patients will experience these side

effects and medications can be given to make them less serious or less uncomfortable. There may also be risks involved in taking this medication that have not been identified in the studies done so far, so please report anything that is troubling you to your trial doctor. Your progress will be closely monitored and your doctor will offer whatever help is available to cope with any side effects observed. Occasionally some patients need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious.

Side effects which are very common (occurring in at least 10 patients out of 100, ≥10%)

- Decrease in red blood cells (anaemia) – this can cause tiredness and breathlessness and you may need a blood transfusion.

- Decrease in platelets (thrombocytopenia) – this may increase your risk of bleeding.

- Decrease in white blood cells (neutropenia and leukopenia) – this can increase your risk of an infection. **You should contact your trial doctor or nurse straight away if you feel unwell or if your temperature goes above 38°**

- Nausea

- Vomiting

Side effects which are common (occurring in between 1 and 10 patients out of 100, ≥1% to <10%)

- Febrile neutropenia (a fever caused by neutropenia – a decrease in white blood cells which can increase your risk of an infection)

- Diarrhoea

There is also a theoretical risk that AZD6738 might make you more sensitive to the sun, so please take care not to get excessive sun exposure whilst taking this drug and take precautions *(e.g. use of high factor sun cream, long sleeved clothing/trousers, wearing a hat etc.)*

There is a risk that AZD6738 might cause you to feel dehydrated, if this happens your doctor might offer you some supportive treatment to help with this.

All drugs have the potential risk of an allergic reaction which if not treated promptly could become life threatening. **You should seek medical advice and contact your trial doctor or research nurse immediately if you have trouble breathing or have swelling of the face, mouth, lips, gums, tongue or neck.**

It is important that you report all symptoms and side effects that you may experience to your trial doctor or research nurse as soon as they occur, whether or not you think they are caused by the trial treatment so they can advise you what to do.

Can I take other medication whilst participating in the AZD6738 treatment cohort?

There are certain groups of medications that you will not be allowed to take while you are in this treatment cohort because of the way they interact with trial treatment. These medications include certain antibiotics, anti-fungal treatments, HIV treatments, anticonvulsant drugs, calcium channel blockers and antidepressants. You should inform your trial doctor of any medications that you are

taking, and if necessary they will try and find an alternative for you. If there is no alternative you may not be able to take part in this treatment cohort. You will not be asked to stop any medications that you need. Some herbal and dietary supplements and some vaccinations may interact with trial treatment, so need to be discussed with your doctor before they are taken.

You should avoid consumption of grapefruit, grapefruit hybrids, pummelos, star-fruit, Seville oranges or products containing the juice of any of these (such as marmalade) during the entire trial and preferably 7 days before the first dose of trial treatment.

If you begin taking any new medications or supplements while participating in the trial, please inform your trial doctor as soon as possible.

Appendix for Cohort C: Olaparib treatment for two weeks before surgery

Important things to know

This appendix contains detailed information on the trial treatment **olaparib** including information on the possible side effects and any specific instructions you will need to follow when receiving trial treatment.

What is olaparib treatment?

Olaparib belongs to a group of drugs known as PARP inhibitors. Blocking PARP with olaparib may prevent the cancer cells from repairing their DNA causing them to die. It is thought that olaparib may be an effective treatment option for patients with TNBC.

How should olaparib be taken?

The treatment is administered during the 2-week window between finishing chemotherapy and before surgery. In this short period of time you will take olaparib every day for 14 days. At the start of the 2-week period of treatment you will be given a sufficient supply of olaparib tablets to take home with you. Olaparib tablets should be taken by mouth twice a day with a glass of water. The tablets should be taken whole and should not be split, chewed, crushed or dissolved. Olaparib tablets can be taken with or without food.

You will need to take a total dose of 600mg per day; this should be taken as two separate doses of 300mg (2 x 150mg tablets) taken at the same time each day approximately 12 hours apart, or as directed by your trial doctor or research nurse. You may take your olaparib tablets up to 2 hours after the scheduled dose time. If you forget to take a dose of olaparib and if more than 2 hours has passed since your scheduled dose time or you are sick shortly after taking a dose of olaparib you should continue to take the next dose as scheduled. You should not take extra tablets to make up a missed dose.

Please store your olaparib tablets at room temperature and out of direct sunlight. There will be some tablets left in the bottle at the end of treatment, and you should bring all bottles (including empty bottles and those containing the leftover tablets) to the clinic visit after completing trial treatment.

How long will I receive olaparib for?

You will received trial treatment for 14 days in the 2-week window after completing your chemotherapy and before surgery, unless you need to stop due to side effects of the treatment.

After surgery your doctor will discuss with you what your next options for treatment are.

What are the side effects of treatment with olaparib?

As with any treatment, olaparib can have side effects. No-one can predict before you begin treatment whether you will have any of these, or how serious they might be. Not all patients will experience these side effects and medications can be given to make them less serious or less uncomfortable. There may also be risks involved in taking this medication that have not been identified in the studies done so far, so please report anything that is troubling you to your trial doctor. Your progress will be closely monitored and your doctor will offer whatever help is available to cope with any side effects observed. Occasionally some patients need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious.

Side effects which are very common (occurring in at least 10 patients out of 100, ≥10%)

- Decrease in red blood cells (anaemia) – this can cause tiredness and breathlessness and you may need a blood transfusion.
- Fatigue
- Physical weakness or lack of energy
- Nausea
- Vomiting
- Diarrhoea
- Indigestion
- Headache
- Taste changes
- Dizziness
- Decreased appetite
- Cough
- Shortness of breath
- Decrease in white blood cells (neutropenia and leukopenia) – this can increase your risk of an infection. **You should contact your trial doctor or nurse straight away if you feel unwell or if your temperature goes above 38°**

The majority of side effects reported in previous studies (as listed above) have been manageable and your doctor will discuss with you what needs to be done in case you experience these or any other side effects while you are taking olaparib.

Please note that if symptoms of physical weakness or lack of energy, fatigue or dizziness occur, you should be careful while driving or using machinery.

Side effects which are common (occurring in between 1 and 10 patients out of 100, ≥1% to <10%)

- Decreased level of white blood cells (lymphocytes) in the blood (lymphopenia)
- Rash
- Abnormalities in kidney function tests which measure how well the kidneys are working (i.e. increase in creatinine).
- A sore mouth
- Abdominal pain
- Venous thromboembolism (when a blood clot forms in one of your veins)
- Decrease in platelets (thrombocytopenia) – this may increase your risk of bleeding

Side effects which are uncommon or rare (occurring in fewer than 2 patients out of 100, <1.5%)

- Hypersensitivity (allergic) reactions
- Dermatitis (eczema)
- Increased volume of red blood cells in the blood
- Inflammation of the lungs (pneumonitis). **If you develop increasing breathlessness or cough please inform your trial doctor.**
- A blood disorder which causes a drop in the number of blood cells (myelodysplastic syndrome (MDS)) or blood cancer (acute myeloid leukaemia (AML), acute erythroid leukaemia, chronic myelomonocytic leukaemia or myeloid leukaemia) which are serious conditions and can be fatal.

- Angioedema
- Erythema nodosum

All drugs have the potential risk of an allergic reaction which if not treated promptly could become life threatening. **You should seek medical advice and contact your trial doctor or research nurse immediately if you have trouble breathing or have swelling of the face, mouth, lips, gums, tongue or neck.**

It is important that you report all symptoms and side effects that you may experience to your trial doctor or research nurse as soon as they occur, whether or not you think they are caused by the trial treatment so they can advise you what to do.

Can I take other medication whilst participating in the olaparib treatment cohort?

There are certain groups of medications that you will not be allowed to take while you are in this treatment cohort because of the way they interact with trial treatment. These medications include certain antibiotics, anti-fungal treatments, HIV treatments, anticonvulsant drugs, calcium channel blockers and antidepressants. You should inform your trial doctor of any medications that you are taking, and if necessary they will try and find an alternative for you. If there is no alternative you may not be able to take part in this treatment cohort. You will not be asked to stop any medications that you need. Some herbal and dietary supplements, and some vaccinations may interact with trial treatment, so need to be discussed with your doctor before they are taken.

You should avoid consumption of grapefruit, grapefruit hybrids, pummelos, star-fruit, Seville oranges or products containing the juice of any of these (such as marmalade) during the entire trial and preferably 7 days before the first dose of trial treatment.

If you begin taking any new medications or supplements while participating in the trial, please inform your trial doctor as soon as possible.

Appendix for Cohort D: Durvalumab treatment for two weeks before surgery

Important things to know

This appendix contains detailed information on the trial treatment **durvalumab** including information on the possible side effects and any specific instructions for you to follow when receiving trial treatment.

What is durvalumab treatment?

Researchers have found that sometimes the body's own immune system may slow down or control cancer growth. Sometimes though, this natural immune system response stops, and the cancer is not killed by the body's own immune system. Research has shown that in some patient's cancer cells and immune cells start to give signals that stop the body's immune system from killing the cancer. One such signal is called Programmed Cell Death Ligand 1 or PD-L1 for short. New drugs like durvalumab work to block this signal and to increase the immune response. Durvalumab is an antibody (a protein produced by the body's defence system) and it is hoped that by blocking this signal, the immune cells will once again be able to prevent or slow down cancer growth. It is thought that patients with TNBC may benefit from durvalumab.

How will durvalumab be given?

Durvalumab is administered at the start of the 2-week window between finishing chemotherapy and before surgery, via intravenous infusion. You will receive one infusion of trial treatment on the first day of this window. A total dose of 1,500 mg will be administered over a period of 1 hour. You will need to come to the hospital for this visit in order to receive the infusion but you do not need to stay in the hospital overnight. You will be closely monitored by your doctor or nurse during the infusion and for 1 hour after the infusion. This will include taking your blood pressure and pulse.

How long will I receive durvalumab for?

You will receive trial treatment on day 1 only of the 2-week period after completing your chemotherapy and before surgery.

After surgery your doctor will discuss with you what your next options for treatment are.

What are the side effects of treatment with durvalumab?

As with any treatment, durvalumab can have side effects. No-one can predict before you begin trial treatment whether you will have any of these, or how serious they might be. Not all participants will experience these side effects and medications can be given to make any side effects less serious or less uncomfortable. There may also be risks involved in taking this medication that have not been identified in the studies done so far, so please report anything that is troubling you to your trial doctor. Your progress will be closely monitored and your doctor will offer whatever help is available to cope with any side effects observed. Occasionally some patients need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious.

Most of the possible side effects listed below are mild to moderate. However, some side effects can be very serious and life-threatening and may even result in death. Some side effects do not need treatment while others generally get better with treatment. Some participants may need to delay doses of durvalumab to allow the side effects to get better. The most important possible side effects, which are listed below, may occur because of the way durvalumab works on the immune system and

they have been seen in participants treated with durvalumab in clinical studies. Side effects like these have also been seen in clinical studies with other drugs that are very similar to durvalumab.

Side effects which are very common (occurring in at least 10 patients out of 100, ≥10%)

- Cough
- Diarrhoea
- Rash/dry itchy skin
- Fever
- Chest infection

- Low thyroid (Hypothyroidism): This is when the thyroid gland produces less thyroid hormone than it should which causes the metabolism to run too slow. Symptoms may include but are not limited to fatigue, increased sensitivity to cold, constipation, dry skin, unexplained weight gain, puffy face, muscle weakness, slow heart rate, thinning hair, impaired memory. The condition can be treated with replacement thyroid hormone.

Side effects which are common (occurring in between 1 and 10 patients out of 100, ≥1% to <10%)

- Inflammation of the lungs (pneumonitis or pneumonia) a serious condition which can be fatal. **If you develop increasing breathlessness or cough please inform your trial doctor.**

- Difficulty speaking (dysphonia)

- Accumulation of fluid under the skin causing swelling, often in the lower legs and ankles.

- Liver problems: Increases in the blood level of substances called enzymes found within your liver cells may occur. The enzyme changes are unlikely to make you feel unwell. However if these blood enzyme levels become very high, your trial doctor may need to stop the trial treatment.

- High thyroid (Hyperthyroidism): This is when the thyroid gland produces too much thyroid hormone. Symptoms include anxiety or nervousness, weight loss, frequent and loose bowel movements, breathlessness, feeling hot and possibly having heart palpitations. Depending on the severity of the symptoms treatment may include just monitoring the symptoms, treating the symptoms themselves and/or giving medicine to block the thyroid hormone.

- Kidney problems: You may have an increase of creatinine levels in a blood test (creatinine is a protein marker that measures kidney function) but not have any symptoms or feel unwell.

- Pain or difficulty urinating (dysuria)

- Night sweats

- Oral thrush

- Dental and soft tissue infections

- Flu
- Muscle pain (myalgia)
- Infusion-related reactions and hypersensitivity/anaphylactic reactions: Reactions may occur during or after the infusion of trial treatment. The reaction may cause fever or chills and a change in blood pressure or difficulty in breathing which might be serious. **Please inform your trial doctor if you experience any of these symptoms even if it has been several days after the infusion has been completed.**

Side effects which are uncommon side effects (occurring in less than 1 patient out of 100, <1%)

- Interstitial lung disease (ILD): 'Interstitial' means the disease affects the interstitium, the lace-like network of tissue that supports the air sacs in the lungs. ILD is a broad term which describes more than 200 different disorders that can cause scarring (fibrosis) or inflammation of the lungs. This scarring or inflammation can cause stiffness in the lungs which may make it difficult to breathe. **Please inform your trial doctor if you experience any difficulties breathing even if it has been several days after the infusion has been completed.**
- Inflammation of the intestine (colitis). It may cause abdominal pain and diarrhoea with or without blood. Fever may be present. It may require you to receive additional fluids. If left untreated, this may lead to a tear in the wall of the intestine which can be serious and life threatening. **Please inform your trial doctor if you have any of these symptoms.** Liver problems: A participant may develop inflammation of the liver called hepatitis, however this is uncommon. Signs and symptoms of this include yellowing of the skin or whites of the eyes, dark urine, severe nausea and vomiting, pain in the upper right side of your abdomen, skin itchiness, not feeling hungry and bleeding or bruising more easily than normal.
- Problems with your adrenal glands (adrenal insufficiency): May cause stomach pains, vomiting, muscle weakness and fatigue, depression, low blood pressure, weight loss, kidney problems, and changes in mood and personality. These complications may be permanent and may require hormone replacement.
- Type 1 Diabetes mellitus (which may present with diabetic ketoacidosis) which may cause increased blood glucose levels (called 'hyperglycaemia'): Symptoms may include weight loss, increased urination, increased thirst, and increased hunger. Type 1 diabetes will require replacement of insulin through injection. **Please inform your trial doctor if you have any of these symptoms.**
- Problems with the pituitary gland (hypopituitarism): Hypopituitarism refers to decreased output of hormones from the pituitary gland in the brain and may be caused by inflammation of the pituitary gland (hypophysitis). Symptoms may include headaches, thirstiness, and trouble seeing or double vision, leakage of breast milk or irregular periods in women. These complications may be permanent and may require hormone replacement.
- Extreme thirst or passing large amounts of urine (diabetes insipidus)
- Inflammation of the kidneys (nephritis) that stops the kidneys from working properly.

- Dermatitis (eczema)
- Pemphigoid (Inflammation of the skin so you may have itching, blistering skin redness, rash, widespread peeling of the skin and possibly ulceration or pustule formation)
- Myasthenia Gravis (A condition that may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing)
- Immune thrombocytopenia (Low platelet count caused by your immune system, this may cause bruising and an increased tendency to bleed)
- Thyroiditis (Inflammation of the thyroid gland an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy)
- Encephalitis (Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behaviour, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness)
- Subcutaneous injection site reaction (inflammation in the skin at the site of injection)
- Immune-mediated neutropenia (low blood immune cell count caused by your immune system acting on some of your white blood cells)
- Immune-mediated cystitis (inflammation of the bladder caused by your immune system attacking some of your bladder cells)
- Sclerosing cholangitis (Inflammation of the bile ducts in your liver)
- Inflammation of the heart muscle (myocarditis) or lining of the heart (pericarditis). Symptoms can include chest pain, rapid or abnormal heart beat, shortness of breath and swelling of your legs. **Please inform your trial doctor immediately if you experience any of these symptoms**.
- Inflammation of the muscles used to move the body (myositis) and muscle weakness (polymyositis).
- Inflammation of the pancreas (pancreatitis). Pancreatitis usually causes symptoms of persistent upper abdominal pain (sometimes made worse by eating and drinking), nausea, vomiting and general weakness. Pancreatitis usually settles with simple measures but it can be a serious condition and can be fatal. **You should immediately tell your trial doctor if you develop any unusual symptoms.** You may get an increase of lipase and amylase levels in a blood test (related to the pancreas) but not have any symptoms or feel unwell. Lipase and amylase are enzymes or protein markers that measure the function of your pancreas. Uncommonly these increases may be associated with pancreatitis.
- Nervous system problems: Symptoms can include unusual weakness of legs, arms, or face, Numbness or tingling in hands or feet. In rare situations there is the potential for the inflammation of the nervous system to be severe: **Tell your trial doctor if you have**

problems swallowing, if you start to feel weak very quickly and you are having trouble breathing.

In addition to the possible risks identified in participants treated with durvalumab, other immune-mediated side effects are possible that have not been observed, and can result in inflammatory side effects in any organ or tissue.

All drugs have the potential risk of an allergic reaction which if not treated promptly could become life threatening. **You should seek medical advice and contact your trial doctor or research nurse immediately if you have trouble breathing or have swelling of the face, mouth, lips, gums, tongue or neck.**

It is important that you report all symptoms and side effects that you may experience to your trial doctor or research nurse as soon as they occur, whether or not you think they are caused by the trial treatment so they can advise you what to do.

Can I take other medication whilst participating in the durvalumab treatment cohort?

There are certain groups of medications that you will not be allowed to take while you are in this treatment cohort because of the way they interact with trial treatment. These medications include but are not limited to certain immunosuppressive drugs and oral steroids. You should inform your trial doctor of any medications that you are taking, and if necessary they will try and find an alternative for you. If there is no alternative you may not be able to take part in this treatment cohort. You will not be asked to stop any medications that you need. Some herbal and dietary supplements, and some vaccinations may interact with trial treatment, so need to be discussed with your doctor before they are taken.

If you begin taking any new medications or supplements while participating in the trial, please inform your trial doctor as soon as possible.

To be printed on hospital headed paper

ICR The Institute of Cancer Research

PHOENIX

CANCER RESEARCH UK

INFORMED CONSENT FORM FOR TRIAL ENTRY

Version 6.0, 27 Oct 2022

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

EudraCT: 2018-002077-21
Sponsor Number: CCR4706

Centre: _____ Clinician: _____

Patient's hospital number: _____ Trial ID Number: _____

Please initial

1. I confirm that I have read and understood the **PHOENIX PATIENT INFORMATION SHEET FOR TRIAL ENTRY, Version 6.0, dated 27 Oct 2022** and have had the opportunity to ask questions and had these answered satisfactorily. ☐

2. I agree to continue to take part in the trial and proceed to **PHOENIX TRIAL ENTRY**. 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 full name, date of birth, postcode, 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 enter the PHOENIX trial. ☐

4. I agree to ICR-CTSU using national records to keep track of my progress and follow up my health status. ☐

5. 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: _____ Trial ID Number: _____

Please initial

6. I agree to my GP being informed about my participation in this trial. ☐
7. I agree to additional blood samples being taken for research as part of this trial and sent to specialist research laboratories in the UK for analysis. ☐
8. I agree to additional tumour tissue samples being collected via biopsies as part of this trial and sent to specialist research laboratories in the UK for analysis. ☐
9. I agree that tumour tissue taken from my breast cancer at surgery and if my cancer comes back, can be used as part of this trial and sent to specialist research laboratories in the UK for analysis. ☐
10. I understand that information collected about me, including genetic details, may be shared with other organisations for the purpose of health and care research, but that I will not be identifiable from this information. ☐
11. If I withdraw from the trial, I consent to my doctor providing authorised researchers with basic clinical information that would be routinely collected and written in my medical records. ***(Optional – please initial Yes or No)***

    Yes ☐ No ☐

12. I consent to my samples 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