To be printed on hospital headed paper

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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 FOR CONTINUATION TO PART 2: COHORTS A & D (DURVALUMAB)

Version: 6.0
Date: 18 Oct 2022

Invitation to continue to Part 2 of the PHOENIX clinical trial

- You have been given this patient information sheet because you already agreed to take part in PHOENIX, may have received durvalumab trial treatment before your surgery (cohort D only), and you may be suitable for Continuation to Part 2 of the trial.
- Before you decide whether to continue to Part 2, 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 **continue to Part 2 of the PHOENIX trial**.

Important things to know

- This information sheet provides information you will need to know to make an informed decision about whether to continue to Part 2 of the PHOENIX trial.
- In this information sheet you will find further details on why we are doing this trial, why you have been invited to continue to Part 2 and what will be involved if you decide to participate further.

ICR The Institute of Cancer Research

CANCER RESEARCH UK

Contents

Why am I being invited to take part in PHOENIX Part 2?

You have been invited to continue to Part 2 of the PHOENIX trial because:

- You previously agreed to take part in PHOENIX and either; received trial treatment with durvalumab (cohort D) or received no trial treatment (cohort A) between completing chemotherapy and having surgery
- Trackable mutations were identified in your tumour tissue sample that you agreed to provide at Trial Registration; so you are suitable to consider continuation to Part 2 of the PHOENIX trial.

Do I have to take part?

No, it is up to you to decide whether or not to continue to Part 2. Your participation is entirely voluntary and you will be given sufficient time to decide whether or not you wish to participate. Your decision to continue to Part 2 or not will not affect the standard of care you receive. If you do decide to take part 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 the trial treatments have been, and will continue to be, monitored closely in this trial. No new safety concerns relating to treatment with durvalumab have been raised in this trial to date so you are now being given the option to continue to Part 2 of the PHOENIX trial to confirm if you are suitable to receive trial treatment after surgery (called the adjuvant setting). The purpose of giving trial treatment in the adjuvant setting is to investigate whether any biological activity that is seen within the residual disease after taking trial treatment in the short 2-week window before surgery is also seen in changes in blood tumour markers after longer exposure to trial treatment over 12 months.

What will happen if I decide to continue to PHOENIX Part 2?

If you agree to continue to Part 2 you will be given this information sheet to keep and you will be asked to sign a consent form for **Continuation to Part 2 of the PHOENIX Trial**.

In order to determine if you may be suitable to resume trial treatment within Part 2, you will be asked to provide a blood sample (30ml which is equivalent to approximately 6 teaspoons) which will be sent to the trial central laboratory at The Institute of Cancer Research and Royal Marsden NHS Foundation Trust where “circulating tumour DNA” or ctDNA screening will be performed.

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.

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". A sample of your tumour tissue has already been tested for trackable mutations and you have been given this information sheet because trackable mutations have been identified in your tumour tissue, which can be used to test for the presence or absence of ctDNA in your blood.

We estimate that it will take approximately 2 weeks for the results to be returned to your trial doctor, although in some circumstances results may take longer. We will also ask for information in your medical records to be provided to us by the research team at your hospital.

In some cases you may be asked by your trial doctor or research nurse to provide a further blood sample in order to complete ctDNA screening. This may happen if the analysis fails due to technical difficulties in the central laboratory or if the analysis needs to be repeated to confirm the result and there is not enough blood left to do so. You are under no obligation to provide a further blood sample, it is your decision as to whether or not you wish to do so however if the result is not confirmed then you will not have the option to receive trial treatment in Part 2.

Based on previous research, we think that approximately a fifth of all PHOENIX participants may have ctDNA identified in the ctDNA screening blood sample collected 30 days or 3 months after surgery.

What will happen if ctDNA is found in my blood sample?

If ctDNA is found to be present in the blood sample you provided for ctDNA screening you will need to have some assessments to check that you are suitable to receive trial treatment in Part 2.

The assessments may all be done together during one visit, or across a few visits. Your doctor will talk to you about this.

The assessments are outlined in the following table:

Pre-treatment assessment	Further details
Imaging (bone scan and CT scan, or FDG PET-CT scan)	You will be asked to have an additional bone scan and CT scan or FDG PET-CT to show whether the cancer has spread to another part of the body: • If the scan shows no evidence that the cancer has spread to other parts of the body, it may be possible for you to receive trial treatment for 12 months in Part 2 provided that you are suitable to receive trial treatment after the assessments listed below have been performed. • If the scan shows evidence that the cancer has spread to other parts of the body, your doctor will be able to discuss treatment options available to you outside the PHOENIX trial.
Review of your current health and medication	To check that you are suitable to receive trial treatment in Part 2.

Pre-treatment assessment	Further details
An electrocardiogram (ECG)	To assess your heartbeat rhythm.
Physical examination	Including weight, blood pressure, heart rate and temperature.
Collection of blood samples for routine tests	Approximately 3 teaspoons (15ml) of blood will be taken for routine safety checks to confirm you would be suitable to receive trial treatment in Part 2.
A pregnancy test	A pregnancy test will be carried out for all women who are able to get pregnant.

What will happen if ctDNA is not found in my blood sample or tests show I am not suitable to receive trial treatment in Part 2?

If ctDNA is not found to be present in the blood sample you provided for ctDNA screening or tests show your cancer has not spread to other parts of the body, but you are not suitable to receive trial treatment in Part 2 we will continue to collect blood samples from you every 3 months for a period of 24 months for research into TNBC.

Timing of blood sample collections for patients not resuming trial treatment		
Type of blood sample	**Amount of blood that will be taken**	**Timing of collection**
Research blood sample to explore ctDNA and biomarkers which may help to predict how well treatment will work for individuals	20ml (4 teaspoons)	Every 3 months for up to 2 years (8 samples in total)

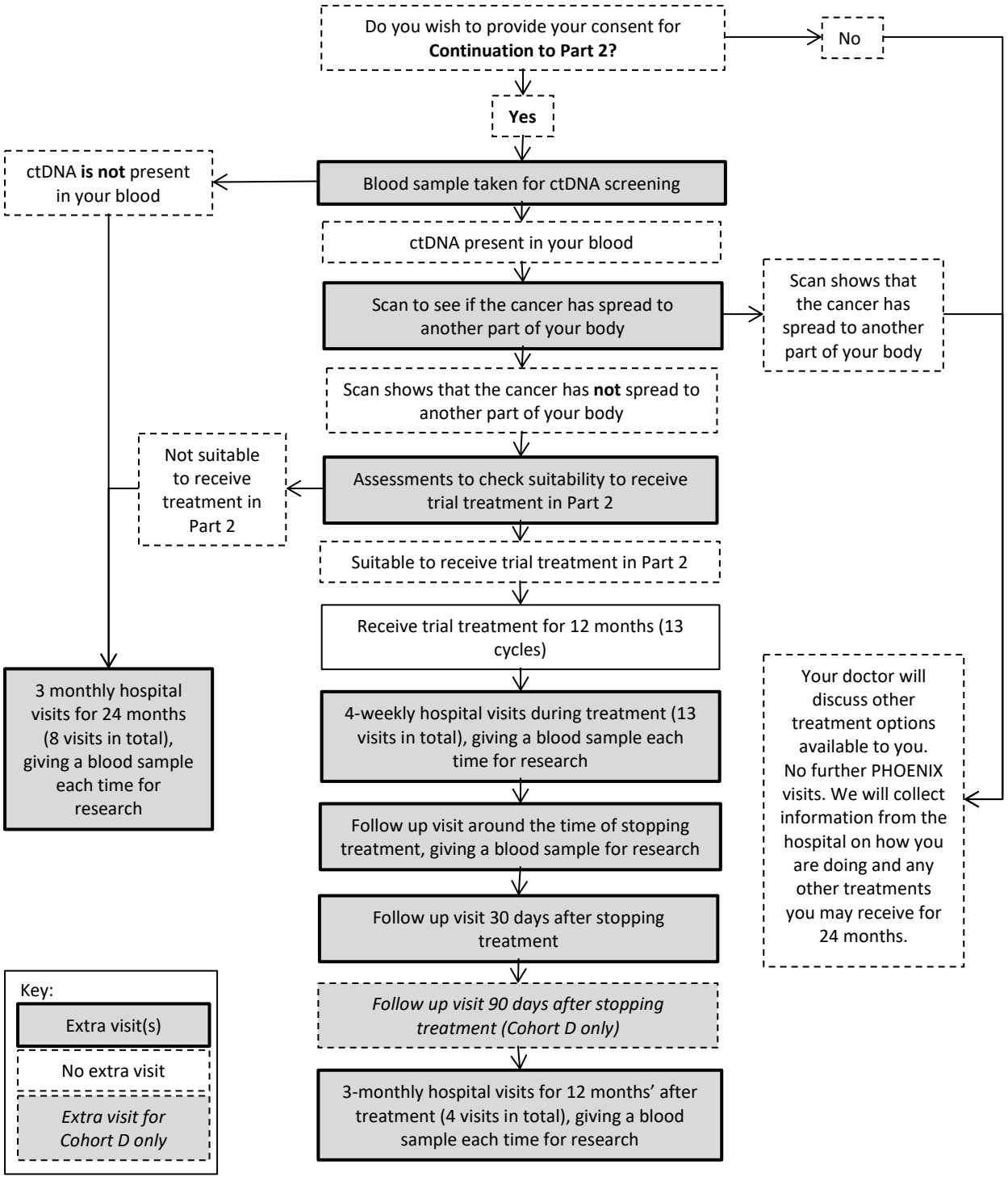
We will also continue to collect information from your hospital on how you are getting on and about any further treatments you may receive in future. If available, we would also like to collect any tissue samples taken as part of your routine care if your cancer comes back once you have finished trial treatment but while you are still being followed up for the trial.

What if I decide that I do not want to take part?

If you decide you do not want to participate any further your doctor will discuss the treatment options available outside this trial with you.

PHOENIX Part 2 Flow Chart

The following flow chart sets out the steps involved if you continue to Part 2. Some steps will involve extra visits to the hospital.



How will durvalumab be given in Part 2?

If you are confirmed as suitable to receive trial treatment in Part 2, you will receive trial treatment in 4 weekly cycles for up to 12 months (13 cycles).

Durvalumab is given via intravenous infusion. You will receive one infusion on the first day of each treatment cycle (13 infusions in total). A total dose of 1,500 mg will be administered over a period of 1 hour. You will come to the hospital for the visit and each infusion but you do not need to stay in the hospital overnight. You will be closely monitored by your doctor or nurse during each infusion. This will include taking your blood pressure and pulse before, during and after each infusion.

How long will I receive trial treatment for in Part 2?

You will receive trial treatment in 4 weekly cycles for 12 months (13 cycles), unless your cancer gets worse (progresses), or you need to stop due to side effects of the treatment.

When you stop taking trial treatment your doctor will discuss with you what your next options for treatment are.

What assessments will be required if I receive trial treatment in Part 2?

You will have regular clinic visits to monitor your progress and any side effects while taking trial treatment in Part 2.

These visits will take place:

- Within 3 days before starting trial treatment in Part 2 (Cycle 1)
- Up to 3 days before starting Cycle 2, before taking your first dose for the next cycle
- Up to 3 days before starting Cycles 3-13, before taking your first dose for the next cycle

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 assessments.

During the clinic visits you will also have regular assessments and routine blood tests, and 13 research blood sample collections, as outlined in the following tables:

<table>
<tr><th colspan="2">Timing of assessments in clinic during treatment</th></tr>
<tr><th>Assessment</th><th>Timing of assessment</th></tr>
<tr><td>Discussion with your trial doctor to document changes in your health or medications since your last visit</td><td rowspan="2">• Within 3 days before starting trial treatment in Part 2
• Up to 3 days before starting cycle 2
• Up to 3 days before starting cycles 3-13</td></tr>
<tr><td>Physical examination including weight, blood pressure, heart rate and temperature</td></tr>
<tr><td>ECG to assess your heartbeat rhythm</td><td>• Up to 3 days before starting cycle 2
• Up to 3 days before starting cycles 3-13</td></tr>
<tr><td>Pregnancy test for all women who are able to become pregnant</td><td>• Up to 3 days before starting cycle 2
• Up to 3 days before starting cycles 3-13</td></tr>
</table>

Timing of blood sample collections during treatment		
Type of blood sample	**Amount of blood that will be taken**	**Timing of collection**
Routine blood tests for routine safety checks	15ml (3 teaspoons)	• Up to 3 days before starting cycle 2 • Up to 3 days before starting cycles 3-13
Research blood sample to explore ctDNA and biomarkers which may help to predict how well treatment will work for individuals	20ml (4 teaspoons)	• Up to 3 days before starting cycle 2 • Up to 3 days before starting cycles 3-13
Research blood samples taken before starting cycles 2–13 will need to be taken before you receive your infusion for that cycle.		
The maximum amount of blood that will be collected for research purposes at any clinic visit is 40ml (8 teaspoons).		

What happens once I stop taking trial treatment?

You will need to visit the hospital when you finish cycle 13 of treatment for assessments to be performed. In case your doctor decides that you should stop treatment earlier than planned, or you decide you want to stop taking treatment for any reason, the assessments might be done at the next planned visit.

You will also need to visit the hospital 30 days and 90 days after the last treatment cycle. At these visits your trial doctor and research nurse will check any medications you are taking, ask if you have any lasting side effects and conduct a physical examination and perform blood tests for routine safety checks.

After you stop trial treatment you will have to attend the hospital every 3 months for a further 12 months (or total of 24 months from your 3 month post-surgery visit if you stop trial treatment early) to have a research blood sample collected. If your cancer comes back during this time, we would also like to collect any tissue samples taken as part of your routine care. After this time we would also like to keep in touch with your doctor to continue to collect information about your health status, ideally we would like to do this for life.

Assessments after stopping treatment		
Assessment	**Further details**	**Timing of assessment**
Medication and symptoms review	Discussion with your trial doctor to document changes in your health or medications since your last visit	• around the time of stopping trial treatment • 30 days after stopping trial treatment • 90 days after stopping trial treatment
Physical examination	Including weight, blood pressure, heart rate and temperature	• around the time of stopping trial treatment • 30 days after stopping trial treatment

		• 90 days after stopping trial treatment
ECG	To assess your heartbeat rhythm	• around the time of stopping trial treatment • 30 days after stopping trial treatment • 90 days after stopping trial treatment
Pregnancy test	For all women who are able to become pregnant	• 30 days after stopping trial treatment

Timing of blood sample collections after stopping treatment		
Type of blood sample	**Amount of blood that will be taken**	**Timing of collection**
Routine blood tests for routine safety checks	15ml (3 teaspoons)	• around the time of stopping trial treatment • 30 days after stopping trial treatment • 90 days after stopping trial treatment
Research blood sample to explore ctDNA and biomarkers which may help to predict how well treatment will work for individuals	20ml (4 teaspoons)	• around the time of stopping trial treatment • at each 3-monthly visit after stopping trial treatment, for 12 months (4 visits) (or total of 24 months from your 3 month post-surgery visit if you stop trial treatment early

What are the side effects of treatment?

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 patients 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 patients 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 out of 100 participants, ≥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 participants out of 100, ≥1% to <10%)

- Inflammation of the lungs (pneumonitis or pneumonia). **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 participant 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 while participating in PHOENIX Part 2?

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.

Will there be anything extra I need to do if I continue to Part 2?

If you decide to continue to Part 2, you will need to:

- Sign the consent form for Continuation to Part 2 to show you understand what participation involves.
- Attend all scheduled appointments.

If the assessments show you are suitable to receive trial treatment, you will also need to:

- Take your trial treatment as directed.
- Only take the trial treatment yourself.
- Talk to your trial doctor or 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.

What are the possible benefits of taking part?

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?

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 7 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 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. 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.

iv. Radiation exposure

By continuing to PHOENIX Part 2 you will have an additional bone scan and CT scan or FDG PET-CT scan if ctDNA is found in the blood by ctDNA screening. These procedures involve some exposure to ionising radiation. In total the additional radiation dose you may receive from this part of the trial would be equivalent to approximately 13 years of background radiation. Ionising radiation can have an adverse effect on the body, including a small increased risk of about 0.2% causing a cancer several years after the exposure. However, in this case the benefits outweigh any such risk as the additional scan will allow your doctor to monitor the progress of your cancer to detect as early as possible if your cancer has grown.

v. Side effects of trial treatment:

Durvalumab is an unlicensed drug, which means that it is regarded as experimental and not all of the 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 patients need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious.

vi. Risks to an unborn child

There could be risks to an unborn child if you receive 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 forms 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.

vii. 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 blood and tissue samples?

We ask that all patients continuing to Part 2 of the PHOENIX Trial donate blood samples for research during the trial. Details of the samples requested throughout PHOENIX are described in the flow chart on page 7 of this information sheet.

We would also like to collect 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.

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

Blood and tissue samples that you donate in the PHOENIX trial 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 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 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 all cases, your confidentially will be maintained.

In addition, we would like to use your 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.

As explained in the PHOENIX Patient Information Sheet for Trial Entry, 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 previously gave your permission during consent for Trial Entry, 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 benefit financially 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 entered the trial, your full name, hospital number, date of birth, postcode and NHS/CHI number was passed to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the trial is being coordinated. You were given a unique Trial ID Number, which is used together with your initials and date of birth on forms that the research staff at your hospital 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.

As explained in the PHOENIX Patient Information Sheet for Trial Entry, 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

As explained in the PHOENIX Patient Information Sheet for Trial Entry, 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 United Kingdom 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 was previously informed about your participation in the PHOENIX trial. This will ensure that your GP knows 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 hospital's 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, and you previously gave your permission, your hospital will 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.

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 research, and the results will be published in a scientific journal as soon as there is enough information to be sure the results are reliable. 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 consent for Continuation to Part 2 of the PHOENIX trial 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

PHOENIX

INFORMED CONSENT FORM FOR CONTINUATION TO PART 2: COHORTS A&D (DURVALUMAB)

Version 6.0, 18 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 CONTINUATION TO PART 2: COHORTS A & D (Durvalumab), Version 6.0, dated 18 Oct 2022,** and have had the opportunity to ask questions and had these answered satisfactorily. ☐

2. I agree to continue to **PHOENIX PART 2**. 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. ☐

Name of Patient	Signature	Date
Name of Researcher	Signature	Date