(To be printed on local hospital headed paper)

ATARI

ATARI: **AT**r inhibitor in combination with olaparib in gynaecological cancers with **ARI**d1A loss or no loss

PATIENT INFORMATION SHEET
COHORT 1A

ATARI: ATr inhibitor in combination with olaparib in gynaecological cancers with ARId1A loss or no loss – Cohort 1A

We are inviting you to take part in a clinical study

- We are inviting you to take part in a clinical trial called ATARI. This trial is for patients diagnosed with relapsed ovarian, endometrial or endometriosis-related clear cell carcinoma. Part 1 of this information sheet tells you the purpose of the trial and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the trial.

- Before deciding to take part, please take time to read this information carefully and discuss it with friends and relatives if you wish. Please ask your study doctor or nurse if there is anything you do not understand or if you want more information.

- Thank you for taking the time to read this information.

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How to contact us

If you have any questions about this study, please talk to your study doctor at
Hospital Department
Hospital
Address
Address
Tel: 01234 XXX XXX

Part One: About the ATARI trial

1 Important information

What is the purpose of this study?

ATARI is a clinical trial that has been designed based on laboratory research which shows that cancer cells with a specific abnormality (mutation) in a gene called ARID1A are more likely to be killed by a new class of anti-cancer therapy called ATR inhibitors. This molecular abnormality ('ARID1A loss') is present more commonly in some specific types ('subtypes') of gynaecological cancers. Research has also shown that some cancers without an ARID1A mutation ('ARID1A no loss') can be killed by ATR inhibitors when these are given together with another type of drug called a PARP inhibitor.

To test this, the ATARI trial is designed to assess the response (tumour shrinkage) in different groups (cohorts) of patients selected based on their cancer cell subtype and the presence of an abnormality in ARID1A. Based on these individual cancer characteristics, some patients will receive an ATR inhibitor drug (called 'ceralasertib') and others will receive an ATR inhibitor plus a PARP inhibitor (called 'olaparib').

In summary, the main aims of the ATARI trial overall are:

- To confirm whether a new drug called ceralasertib is effective, either on its own or in combination with another drug called olaparib, against relapsed ovarian, endometrial or endometriosis-related clear cell carcinoma.
- To confirm if a particular group of patients are more suitable for treatment with ceralasertib, or ceralasertib in combination with olaparib, than others.

This trial will run internationally, including the UK, France and Canada.

Why am I being invited to take part?

You have been invited to participate in the ATARI study because you have been diagnosed with relapsed ovarian, endometrial or endometriosis-related clear cell carcinoma, that has worsened after platinum (eg carboplatin) based chemotherapy. You also previously agreed to join the initial screening part of this trial, which confirmed you have an abnormality of a protein called ARID1A ('ARID1A loss'). This abnormality is found in the tissue of your cancer; it is not the sort of abnormality which can be passed on to your family.

'ARIDIA loss' in your ovarian, endometrial or endometriosis-related cancer may mean that treatment with a drug called ceralasertib can help control the cancer and is a potential alternative to chemotherapy. Therefore we are inviting you to take part in **ATARI Treatment Cohort 1A**, which is investigating treatment with ceralasertib in patients with relapsed ovarian, endometrial or endometriosis-relatedclear cell carcinoma, who have ARID1A loss.

Approximately 10 patients with the ARID1A loss identified in their screening tissue sample will be invited to participate in Treatment Cohort 1A, with further patients invited to participate if the initial results are promising.

Do I have to take part?

No, it is up to you to decide whether or not to take part in ATARI Treatment Cohort 1A. Your participation is entirely voluntary and you will be given sufficient time to decide if you wish to participate. Whether or not you decide to take part will not affect the standard of care you receive.

If you do decide to take part you will be given this patient information sheet and consent form to read carefully and to sign. A copy of the signed patient information sheet and consent form will be provided to you for your records. If you do decide to take part, you are still free to withdraw from study treatment or from the study at any time. You do not have to give a reason.

Provided you agree, your GP will be informed about your participation in this study. You will receive a card, which indicates that you are participating in a clinical study.

2 What do I need to know about the medicine used in this study?

What is ceralasertib and how does it work?

Ceralasertib is an unlicensed drug being tested in this study and is made by a pharmaceutical company called AstraZeneca (AZ). Ceralasertib works differently to chemotherapy and radiotherapy. Ceralasertib belongs to a new group of drugs known as ATR inhibitors. Laboratory research shows that cancer cells with an abnormality in the ARID1A protein are more likely to be killed by ATR inhibitors. ATR (ataxia telangiectasia and Rad3-related protein) proteins detect damage to DNA in cells and help stop these cells multiplying. ATR inhibitors work by inhibiting growth in tumour cells that use the ATR protein for DNA repair. Ceralasertib is currently being studied to see if it is effective in treating different types of cancer and to see what side effects it may cause.

How should ceralasertib be taken?

Ceralasertib comes as a tablet. At the start of each treatment cycle you will be given a sufficient supply of ceralasertib tablets to take home with you. Ceralasertib tablets should be taken by mouth twice a day as below;

- You should not eat any food for 2 hours before and 1 hour after taking your tablets.
- The tablets should be taken whole and should not be split.
- You will need to take four **tablets per day**; this should be taken as two separate doses of two tablets taken at the same time each day (approximately 12 hours apart).
- You will do this every day for Days 1–14 of a 4 week block, or as directed by your study doctor.
- You may take your ceralasertib tablets up to 2 hours after the scheduled dose time.
- Each 4-week block will be one treatment cycle.
- If you forget to take a dose of ceralasertib and if more than 2 hours has passed since your scheduled dose time, or you are sick shortly after taking a dose of ceralasertib, 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 ceralasertib tablets at room temperature and out of direct sunlight. There will be some tablets left in the bottles at the end of each treatment cycle, and you should bring all bottles (including empty bottles and those containing the leftover tablets) to each clinic visit.

3 What happens during the trial?

What will my taking part in the trial involve?

If you agree to take part you will be given this information sheet to keep and you will be asked to sign a consent form for entry into ATARI Treatment Cohort 1A. You will need to have some assessments before

you can join the treatment cohort. Some of these tests are routine, but others will need to be done to make sure that it is safe for you to take part and that you are suitable for the treatment cohort. These assessments will only be performed after you have agreed to take part by signing a consent form. They may all be done together during one visit, or across a few different visits. Your study doctor will talk to you about this.

What screening assessments will be performed?

The assessments are outlined in the following table:

Assessment	Further details
Collection of a sample of your tumour	This will have been done as part of the initial screening phase of the trial to assess your cancer sample's ARID1A status.
Full review of your medical history	To check that you are suitable to enter **Treatment Cohort 1A.**
Physical examination	Including checking your height, weight, heart rate, blood pressure, temperature and oxygen saturations.
Evaluation of ECOG status	For routine safety checks. The study doctor will assess how your disease is affecting your daily living and abilities; this is undertaken via a series of questions and observations by the study doctor.
An electrocardiogram (ECG)	To assess your heartbeat rhythm. You will need to have three ECGs in a row to ensure that the assessment is as accurate as possible.
Collection of blood samples	Approximately 4 teaspoons (20ml) of blood will be taken for routine safety checks.
A urine dipstick test	For routine safety checks.
A pregnancy test	A pregnancy test will be carried out for all women who are able to get pregnant.

What happens if I am eligible for the study?

If your screening test results show that you are suitable for entry into Treatment Cohort 1A and you agree to continue in the trial, we will ask you to attend the clinic for the first cycle of treatment. You will undergo some baseline assessments (as described in the table below) before beginning treatment with ceralasertib. Trial treatment will be administered in 4-week cycles. During this time you will be taking ceralasertib for the first 14 days of each cycle. You will be required to attend regular hospital appointments so that we can see how your cancer responds to the treatment as well as monitor any side effects you may experience.

If you are not eligible for the study: If your screening tests results show you would not be suitable for or you decide you do not want to participate in treatment cohort 1A your study doctor will discuss the treatment options available outside of this trial with you.

What happens next and what assessments will take place during the trial?

If you are suitable for the trial based on the screening assessments and wish to continue with your participation in ATARI, you will be enrolled into the main study and will be allocated a unique study number.

While you are receiving trial treatment you will see one of the study doctors at regular clinic visits to monitor your progress and any side effects. These visits will take place as follows:

- At the start of treatment (Cycle 1 Day 1),
- After 1 week (Cycle 1 Day 7),
- After 2 weeks (Cycle 1 Day 15),

- After 4 weeks (Cycle 2 Day 1),
- After 6 weeks (Cycle 2 Day 15),
- After 8 weeks (Cycle 3 Day 1)
- At 4 weekly intervals thereafter (Day 1 of each subsequent 4-week treatment cycle).

Clinic visits will also take place when you stop receiving trial treatment, and 30 days after the last dose of treatment. During the clinic visits you will have regular assessments as outlined in the following tables:

At every clinic visit
Physical assessment, including checking your height, weight, heart rate, blood pressure, temperature and oxygen saturations.
Discussion with your study doctor to document changes in your health or medications since your last visit and also a review of the trial medication you have taken
ECOG assessment
Approximately 4 teaspoons (20ml) of blood will be taken for routine safety checks, this may also include coagulation and CA125 tests.
Approximately 4-8 teaspoons (40ml for the first sample and 20ml for samples thereafter) of blood will be taken for research purposes.
A urine dipstick test for routine safety checks if clinically needed

Timing of other assessments in clinic	
Assessment	**Timing of assessment**
A pregnancy test for all women who are able to get pregnant	Before starting trial treatment on Cycle 1 Day 1 and at the start of each new cycle
ECG to assess your heartbeat rhythm	On Day 1 of every cycle and at the end of treatment visit. You will need to have three ECGs in a row to ensure that the assessment is as accurate as possible.
CT and/or MRI scan to assess disease status	Every 8 weeks until the end of your treatment
Research bloods	On Day 1 of every cycle and at the end of your treatment
Image guided biopsy (optional)	On Cycle 1 Day 1 before you start treatment and also at the end of your treatment
Ascites collection (optional)	At any point if clinically needed. Your study doctor will discuss this further with you.

Timing of blood sample collections in clinic		
Type of blood sample	**Amount of blood that will be taken**	**Timing of collection**
Routine blood tests for safety checks	4 teaspoons (20ml)	At your clinic visit
Research blood sample to explore biomarkers which may help to predict how well treatment will work for individuals	Around 4-8 teaspoons (40ml for the first sample and 20ml for samples thereafter)	At your clinic visit

Timing of blood sample collections in clinic
The research blood samples will need to be taken before you receive your treatment on the day of the visit, so you should wait to take your tablets until after your blood samples have been collected.
The maximum amount of blood that will be collected for research purposes at any clinic visit is less than 8 teaspoons (less than 40ml).

After you have completed trial treatment you will continue to have regular assessments in clinic as outlined in the following table:

Follow up assessments in clinic	
Discussion with your study doctor or nurse to document changes in your health or medications since your last visit	30 day follow up only
ECOG assessment	30 day follow up only
Bloods and urinalysis for routine safety checks if clinically indicated	30 day follow up only
CT and/or MRI scan to assess disease status	Every 8 weeks from the safety follow up (for up to 1 year), then every 12 weeks

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

What are the side effects of treatment with ceralasertib?

As with any treatment, ceralasertib 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. Ceralasertib 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 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 study doctor. Your progress will be closely monitored and your study doctor will offer whatever help is available to cope with any side effects observed.

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

- Decrease in red blood cells (anaemia) – this can cause tiredness and breathlessness and you may need a blood transfusion
- Decrease in white blood cells (neutropenia) – this can increase your risk of an infection
- Decrease in platelets (thrombocytopenia) – this may increase your risk of bleeding

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 study doctor or research nurse immediately if you have trouble breathing or have swelling of the face, mouth, lips, gums, tongue or neck.

There is also a theoretical risk that ceralasertib might make you more sensitive to the sun, so please take care not to get excessive sun exposure whilst taking this drug.

It is important that you report all symptoms and side effects that you may experience to your study 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 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 study 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 study doctor before they are taken.

You should avoid consumption of grapefruit, grapefruit hybrids, pomelos, star-fruit, Seville oranges or products containing the juice of each (such as marmalade) during the entire trial and preferably for 7 days before the first dose of study medication.

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

How long will I receive trial treatment for?

Trial treatment will continue to be given to you in 4 weekly cycles unless your cancer gets worse (progresses), or you need to stop due to side effects of the treatment or for any other reason. When you stop taking trial treatment your study doctor will discuss with you what your next options for treatment are. You may however decide to stop your participation in the trial at any time. This means that the length of time each patient is in the study will vary.

What else will happen to me during the trial?

You will be able to continue day-to-day activities as normal during the trial. You will need to attend the clinic visits and have other tests such as the CT/MRI scans as described. Some people may not feel like driving after having tests such as a CT scan; we recommend that someone comes with you when you attend for your hospital appointments.

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

- Sign the consent form for entry into Treatment Cohort 1A to show you understand what participation involves.
- Undertake a biopsy (optional consent)
- 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 study doctor or pharmacist as directed on the label.
- Keep your treatment out of the reach of children.
- Talk to your study 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 study doctor or research nurse as soon as they occur, whether or not you think they are caused by the trial treatment.
- **Tell your study 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 study doctor about any medical problems you have.
- Return any medicine containers (with any leftover tablets) to the trial team at each visit.

4 What are the possible advantages and disadvantages of taking part?

What are the benefits of taking part?

Your study doctor thinks that treatment with ceralasertib may be effective but there is no guarantee of this. The information we gain from this trial may help us to improve treatments for patients with ovarian, endometrial or endometriosis-related cancer in the future.

What are the possible disadvantages of taking part?

Side effects

Ceralasertib is an unlicensed drug, which means that it is 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 study 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.

Risks to an unborn child

There could be risks to an unborn child in this treatment cohort; therefore, if you are pregnant you cannot take part in the trial. If you become pregnant during the trial, these risks could affect you or your unborn child. Before entering the treatment cohort, pregnancy tests will be carried out for all women who are able to get pregnant. If applicable, you must agree to use highly effective forms of birth control from entry into the trial and for 30 days after the last dose of study treatment. Highly effective forms of birth control include:

<u>Non-hormonal birth control methods:</u>

- Total sexual abstinence ie, refrain from any form of sexual intercourse in line with the patients' usual and/or preferred lifestyle. Abstinence must be for the total duration of the study treatment and for at least 1 month (for female patients) or 3 months (for male patients) after the last dose of study treatment. Periodic abstinence (eg, calendar ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.
- Vasectomised sexual partner. With participant assurance that partner received post-vasectomy confirmation of azoospermia.
- Tubal occlusion
- Intrauterine Device Provided coils are copper-banded.

<u>Acceptable hormonal methods:</u>

- Etonogestrel implants (eg, Implanon®, Norplant®)
- Normal and low dose combined oral pills
- Hormonal shot or injection (eg, Depo-Provera)
- Intrauterine system device (eg, levonorgestrel-releasing intrauterine system -Mirena®)
- Norelgestromin/ethinyl estradiol transdermal system
- Intravaginal device (eg, ethinyl estradiol and etonogestrel)
- Cerazette (desogestrel). Cerazette is currently the only highly efficacious progesterone based pill.

One of these methods must be used PLUS male condom. These should be discussed with your study doctor. If you think you may be pregnant, you must tell your study 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.

Additional blood tests and biopsies
You will have more blood tests and potentially additional biopsies if you enter the trial than if you were not taking part. Risks linked with blood sampling include pain from the needle being inserted, light-headedness, possible fainting and (occasionally) infection. The taking of a biopsy may cause some pain, redness, swelling and slight bruising at the biopsy site and (occasionally) fainting. There is a small risk of bleeding, infection and wound healing problems following your biopsy (further details on the risks of the biopsy procedure are provided in Section 2 of this information sheet).

Heartbeat and heart function assessments
The electrocardiogram (ECG) for the electrical tracing of your heartbeat involves placing small electrodes on the surface of your skin. Occasionally, a slight redness or inflammation may appear due to the adhesives used to attach the electrodes to the skin.

Radiation exposure
If you take part in this study you will have CT or MRI scans and you may have CT guided biopsies. Some of these will be extra to those that you would have if you did not take part. CT scans use ionising radiation to form images of your body which provide your doctor with clinical information or enable biopsy procedures to be carried out. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. In patients with your current clinical condition, the chance of this happening to you is extremely small.

Additional hospital visits and travel
You may need to attend hospital more frequently than you would if you decided not to participate in this treatment cohort. 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.

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

5 Further information about taking part

Will my GP be involved?
Your GP will be informed about your participation in the ATARI trial and specifically entry into Treatment Cohort 1A. 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 happens when the research study stops?
You will be given the study drug until your study doctor thinks you are no longer gaining any benefit from treatment or you are going to start on a new treatment for your cancer. The study doctor may decide that your participation in the study is no longer in your best interest and you will be withdrawn from study treatment or from the study. When you stop taking part in the study, you must go through the study withdrawal procedures that the study doctor considers necessary for your safety. Your participation in the study may also be stopped by the study sponsor, ethics committee, or the regulatory authorities. If your study treatment is stopped, by either the sponsor, your study doctor or at your own request, your

study doctor will arrange your continuing care.

What alternative treatments are there?

If you do not want to take part in the study there may be other treatment options available. These may include other experimental anti-cancer drugs, chemotherapy and radiation therapy. There is also supportive care without anti-cancer treatment. Study staff will discuss these alternative treatments and the risks and benefits associated with these treatments with you before you decide to take part in this study.

This completes Part 1 of the Information Sheet.

Please read the additional information in Part 2 before making your decision.

Part Two: General information

6 General information about how the ATARI trial is conducted

What sort of samples will I be asked to donate?

As explained in Section 1, if you agree to join ATARI Treatment Cohort 1A you will be asked to donate extra blood samples for research. Having research blood samples collected is an essential part of participation in this trial. Details of the samples requested are described in Part 1 of this information sheet.

Ascites (fluid build-up)

You may also be asked to provide a sample of ascitic fluid if your doctor thinks you need drainage of ascites for medical reasons. Some patients with ovarian, endometrial or endometriosis-related cancer can develop a build-up of fluid in their abdomen, called ascitic fluid. This may need to be drained by your doctor if it becomes uncomfortable or troublesome. This is not related to taking the study drug and would only be done for medical reasons, not specifically for the trial. However, if you need this procedure as part of your standard care whilst taking part in the trial you will be asked if we can keep some of the fluid as it contains biological information about your cancer that could be used in future research.This is an optional consent within the trial which you do not have to agree to if you do not wish and you can still take part in the study. Please initial the appropriate part of the consent form if you agree to any ascitic fluid collected being used in the trial.

What does having ascitic drainage involve?

Doctors usually treat ascites by making a small cut in the tummy and inserting a tube to drain the fluid. A doctor will usually put in the tube at the hospital. Sometimes they use an ultrasound scan to help them position the tube. Once you are lying down comfortably, the doctor will clean the skin on your tummy. They will give you an injection of local anaesthetic to numb the area so the procedure won't be painful. They will make a small cut in the skin of your tummy and insert a thin tube. The fluid drains out of your tummy and collects in a drainage bag. The tube is covered with a dressing. Sometimes, the doctor may use a couple of stitches to hold it in place. You may have had this procedure undertaken previously as standard of care prior to you entering the trial.

Ascitic drainage may be conducted at any time during the course of the trial as clinically indicated. If ascitic drainage is conducted as part of clinical care, with your consent a sample of fluid should be retained for use in future research.

Tissue Biopsies

We would also like to collect two additional biopsies from you during the course of this trial – one biopsy prior to you starting trial treatment (Cycle 1 Day 1) and one biopsy at the end of your trial treatment. These biopsies are optional and you can decide whether you would like to have these additional procedures performed or not; you can agree to have one or two biopsies performed, or none at all. Please initial the appropriate part of the consent form if you agree to the collection of these samples. Whilst these biopsies are optional, they are an important aspect of this study. The samples we collect will help us to further understand the effect of ceralasertib on your cancer and identify specific features in the cancer that can predict responses to treatment. The tissue collected might help us in the future to predict which patients will benefit from ceralasertib treatment.

What does having a biopsy involve?
A biopsy is the removal of a small piece of tissue from the tumour. All biopsies in ATARI will be taken using a biopsy needle through the skin. The doctor will usually collect 2–4 samples and the whole procedure should take about 30 minutes to do.

Your doctor will discuss the best way to obtain a biopsy in your case. The biopsy site will depend on the accessibility of the site to minimise any risk involved. The biopsy may be done by a surgeon or a radiologist, who may use an ultrasound or CT scan to see where the tumour is. You may have an anaesthetic first to numb the area. It may still be painful or a little uncomfortable afterwards, but mild painkillers such as paracetamol should help.

Irrespective of how the biopsy is performed, this will be done under sterile conditions using standard biopsy procedures in place at your hospital. The risks of biopsies include infection at the site of biopsy, although with proper sterilisation this complication is very rare. The biopsy may also be uncomfortable and bruising at the biopsy site or bleeding from the puncture wound may occur. The chance of minor bruising or bleeding is increased if you are taking aspirin, clopidogrel, anti-blood clotting medication (anti-coagulants) such as warfarin, and/or non-steroidal anti-inflammatory drugs such as ibuprofen. Depending on the site of the biopsy there may be a risk of damage by the biopsy needle to the surrounding area. Therefore tissue samples will be obtained only when it is safe for you and practical to do so. An allergic or other unwanted reaction to the numbing or sedative medicine used in the procedure may also occur.

Additional risks of a biopsy depend on the area of the body being biopsied. Biopsies will be done in different ways in different patients, therefore the specific risks and how likely they are to occur will vary according to the biopsy type, the type of anaesthetic and your general health. The doctor performing the biopsy will talk to you about the risks associated with the biopsy in your individual case.

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.

What will happen to any samples I give?
Any samples you donate will be used to help us understand how your specific type of tumour reacts to treatment with ceralasertib. If we can understand why some patients react to their treatment differently, this knowledge could help other patients in the future. We also hope to find biological markers that may help to predict how well treatment will work for individuals. This will involve looking at the genetic information (DNA) in the samples we collect from you and at any changes in response to treatment. You will not be provided with information from any of the tests conducted on your samples.

The group of medical professionals overseeing the ATARI trial will also oversee the biological sample collection. Your samples may be labelled with your trial ID and date of birth when they are sent to the research lab. When they arrive at the laboratory they will be coded and personal details removed. The coding will maintain your confidentiality whilst allowing biological details to be compared to treatment findings.

The tumour samples will be stored securely in a biobank at the Centre for Molecular Pathology at The Royal Marsden/Institute of Cancer Research. Much of the blood and tumour sample analyses previously described will be conducted in The Institute of Cancer Research Laboratory, but some of the samples may also be sent to other research institutes or companies approved by The Institute of Cancer Research for the respective analyses. In all cases, your confidentially will be maintained.

You are asked to give permission for possible future research using your biological samples, once all of the trial-specific tests are complete; this may involve your samples being sent to institutions outside the European Economic Area (EEA). The confidential nature of these samples and associated data will be fully protected, and any other research using your tissue will first be reviewed and approved by an ethics committee.

How will confidentiality be maintained?

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

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

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

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

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

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

All information which is collected about you during the study will be kept strictly confidential. When you join the trial, your full name, hospital number, date of birth, postcode and NHS/CHI number will be passed to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the study is being coordinated. You will be given a unique trial ID number, which will be used together with your initials and date of birth on forms that the research staff at your hospital will send to ICR-CTSU. All information about you will be stored securely. It will be treated

as strictly confidential and nothing that might identify you will be revealed to any third party. Only members of the research teams at your hospital and the ICR-CTSU will have access to the information that could allow this trial ID number to be linked to you.

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

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

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

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. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.
Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee

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

What 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 study at any point without giving a reason. If you withdraw from the trial, it will not affect the standard of care you receive. Your study doctor will discuss alternative treatment with you and offer you the most suitable treatment available.

If you should withdraw fully from the study, study data collected before your withdrawal may still be processed along with other data collected as part of the clinical study. However no new data will be added to the study database and you may request that all retained identifiable samples are destroyed to prevent future analysis.

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 treatment, we would like your permission for your hospital to send information on your progress to the Trials Office. This is so that the overall quality of the trial is not impaired.

What if there is a problem?

If you have any concern about any aspects of the study you should ask to speak with your study doctor or research nurse who will do their best to answer your questions (contact details in part 1). If you remain unhappy and wish to complain about any aspect of the way you have been approached or treated during the course of this trial, the normal National Health Service complaints mechanisms are available to you. We recommend that you obtain a copy of your hospitals complaints procedure or policy if you intend to make a complaint. Concerns should be raised by speaking to a member of staff at your hospital or by talking to the local Patient Advice and Liaison Service (PALS), which has been established in every NHS Trust and Primary Care Trust (PCT). The details for your hospital are: *[Insert appropriate name for hospital PALS]:* To find out more about this, ask a member of staff, look on the hospital or trust's website, or contact the complaints department for more information.

Your progress will be watched closely and you will be offered 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. If this were to happen, full details of what has happened will be reviewed carefully by the consultant oncologist who has overall responsibility for the ATARI trial. These details may also be sent to the MHRA who oversee the safety of people who take part in any research involving drugs. We may also need to send this information to the ethics committee who approved the trial, all the study doctors who are responsible for patients in this study, and to AstraZeneca (AZ). We are required to provide this information to these parties by law, but you will not be identifiable in any of the information that is sent, and all information will be kept confidential.

Healthcare professionals working on clinical trials are covered by NHS Indemnity and if you are harmed by taking part in this trial you may have grounds for a legal action, but you may 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, that resulted in severe and/or permanent disability, you may be able to claim compensation from The Institute of Cancer Research as Sponsor of the ATARI 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 will happen to the results of the clinical 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. The results will help to decide how to treat advanced gynaecological cancers 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 information becomes available?

Sometimes we get new information about the treatment being studied, which may affect your willingness to continue in the study. If this happens, your study doctor will tell you in a timely manner and discuss whether you should continue in the study. If you decide to continue in the study, you may be asked to sign an updated informed consent form. If you decide to discontinue, your study doctor will make arrangements for your future care.

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

Who is organising and funding the research?

The Chief Investigator of the trial is Dr Susana Banerjee, who is based at The Royal Marsden NHS Foundation Trust, London (also the lead site for the trial). The research trial is being carried out by a network of doctors across the UK and internationally. The trial is co-ordinated by The Institute of Cancer Research Clinical Trials & Statistics Unit (ICR-CTSU). The research is approved and funded by AstraZeneca (AZ), the company who manufacture ceralasertib and who are supplying the drug free of charge. The Lady Garden Foundation charity has also provided funding to support the trial.Your study doctor will not personally receive any payments for including you in this research trial.

Will I be compensated?

No, there is no compensation for participating in this trial. We are also unable to reimburse any travel costs incurred as part of your participation.

Who has reviewed the trial?

The trial has been approved by the Health Research Authority (HRA), a Research Ethics Committee *(insert ethics committee here)*, the UK Regulatory Agency (Medicines and Healthcare Regulatory Agency, MHRA) and the study sponsor's committee for clinical research. This patient information sheet and consent form have been reviewed by the patient review panel in Royal Marsden NHS Foundation Trust.

What do I have to do now?

You will have some time to think about the trial and make your decision. You may wish to discuss it with your GP, family or friends. Please keep this information sheet and a copy of the signed consent form. If, at any time, you have any questions about the trial you should contact your consultant.

7 Useful contact information

Who else can I contact for further information?

You have the right to ask questions about this study at any time and are encouraged to do so. You can call the study doctor or hospital if you feel that you are developing any unwanted side effect, or if you believe you have been injured as a result of your receiving study treatment, or if you have any questions about this study or your participation in this study.

Your study doctor is: _____

Your study nurse is: _____

Contact phone numbers: _____

Out of Hour Numbers: _____

Macmillan Cancer Support is a registered charity providing information, emotional support and publications about all aspects of cancer for cancer patients and their families. They have published useful information about (1) ovarian and endometrial cancers (2) cancer treatments and (3) clinical trials in general. You can contact one of their specialist cancer nurses on their freephone number, 0808 808 00 00 or look on their internet website: (http://www.macmillan.org.uk/Home.aspx).

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

Appendix 1 - Description of Scans

Computed Tomography (CT): CT scan uses x-ray equipment to take pictures of the inside of your body to evaluate the extent of the cancer. It involves you lying down and keeping still on the scanner table for about 20 minutes. Usually, an intravenous agent is injected into your vein to obtain clearer pictures and you may also have to drink an oral contrast agent. You may experience discomfort related to lying still while the CT scan is being carried out.

Magnetic Resonance Imaging (MRI): MRI scans use magnetic and radio waves to take pictures of the inside of your body. Although there is no x-ray exposure, the procedure takes longer (40 minutes to an hour) and involves keeping still while lying down on the scanner table. It can be noisy and you will be in a narrower tunnel compared to CT. Some patients may feel claustrophobic and may experience discomfort related to lying still in an enclosed space for a prolonged period of time while the MRI scan is being taken. A MRI will only be performed if your disease is better visualised on an MRI scan rather than a CT scan.

IRAS number : XXXXXX REC Ref: XX/XX/XXX

Patient's Hospital Number: Trial Entry number (ID):

Name of clinician: Centre:

ATARI: ATr inhibitor in combination with olaparib in gynaecological cancers with ARId1A loss or no loss

ATARI COHORT 1A CONSENT FORM

Please initial to confirm

1. I confirm that I have read and understand the ATARI Cohort 1A information sheet *version __ dated ___/___/___* for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
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.	☐
3. I agree to take part in the ATARI trial. I understand that this will require further tests to confirm eligibility.	☐
4. I consent to having research blood samples collected.	☐
5. I understand that my samples may be labelled with my trial ID number and date of birth when they are sent to the Institute of Cancer Research and Royal Marsden Hospital. My tissue sample will also be labelled with my hospital pathology number.	☐
6. I understand that my clinical samples may be sent to other institutions as explained in the Patient Information Sheet.	☐
7. I understand that sections of any of my medical notes may be looked at by responsible individuals from the research team, from regulatory authorities, ethics committees, Astra Zeneca (the pharmaceutical company who manufacture ceralasertib) and third parties approved by ICR-CTSU or from the NHS Trust where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐
8. I agree to my GP being informed about my participation in this trial.	☐
9. I agree that data will be passed to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) and that my name, date of birth, hospital number, post code and NHS number (CHI number in Scotland) will be given when I join the trial. Thereafter I will be identified by a unique trial number, initials and date of birth. I agree to ICR-CTSU using NHS and national health and registration data to keep in touch with me and follow up my health status. I consent to the sharing of this data.	☐

10. I consent to the collection of fresh tissue biopsies to be taken prior to starting treatment (when commencing first day of treatment) and at the end of all treatment. (**optional**)	Yes ☐	No ☐
11. I consent to having ascitic drainage collected (**optional**)	Yes ☐	No ☐
12. I consent to my samples being stored for possible future research, with the understanding that the confidential nature will be protected, and that ethics committee approval will be obtained before any future research is conducted (**optional**).	Yes ☐	No ☐
13. I consent to the possible future sharing of information collected about me, including biological material, with other organisations which may be outside the European Economic Area (EEA), with the understanding that I will not be identifiable from this information (**optional**).	Yes ☐	No ☐

_____	_____	_____
Name of patient	Signature	Date

I confirm that I have explained the nature, purposes and foreseeable effects of the trial to the subject whose name is printed above.

_____	_____	_____
Name of person taking consent	Signature	Date

_____	_____	_____
Name of researcher (if different from above)	Signature	Date

One copy for participant, one copy for medical records and original to be kept in site file