(Form to be on hospital headed paper)

THIS STUDY HAS BEEN REVIEWED AND APPROVED BY A RECOGNISED RESEARCH ETHICS COMMITTEE

INFORMATION SHEET FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

Title of Project: PARP Inhibitor Resistance Study (PAIRS) COHORT A

IRAS ID: 297051

Introduction

We would like to invite you to take part in our research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives, and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part.

Why have I been invited to take part?

You have been invited to take part in this study because you have received treatment for ovarian cancer and you are about to start, or have recently started, treatment with a drug known as a PARP inhibitor.

Do I have to take part?

No, taking part in the study is entirely voluntary. It is up to you to decide whether or not to take part. If you *do* decide to take part, you will be given this information sheet to keep and asked to sign a consent form. You are still free to withdraw at any time without giving a reason. This will not affect the quality of care you receive.

Taking part in this study will have no effect on the treatment decisions you make with your consultant.

If you decide *not* to take part in the study, it will not affect the quality of your treatment in any way.

Part 1 – What's Involved: Tells you the purpose of this trial and what will happen to you if you take part.

Part 2 – Supporting / Further Information: Gives you more detailed information about the study.

PART 1 – WHAT'S INVOLVED

What is the purpose of the study?

The purpose of the PAIRS study is to collect tumour samples from women who are treated with PARP inhibitors and then analyse them to understand why some women benefit from PARP inhibitor therapy while others do not. This would enable us to use PARP inhibitors in a more personalised way, sparing patients unlikely to benefit from the side-effects of PARP inhibitors, while ensuring those who will benefit receive PARP inhibition therapy.

What does the study involve?

This is a sample collection study. Access to your archival pre-PARP inhibitor tumour sample will be requested. Blood samples will be taken from you, along-side your routine bloods tests. A biopsy will be taken if your cancer gets worse during treatment with a PARP inhibitor. Clinical information about your cancer will be recorded while you are on a PARP inhibitor and subsequent treatments. The samples will be examined in the laboratory to learn more about markers that predict sensitivity and resistance to PARP inhibitor therapy.

The study is planned to recruit a total of 200 patients over 3 years. If you decide to participate in the study, you would be asked to take part until the end of the study if your cancer does not get any worse during that time, or until 6 months after you stop PARP inhibitor if your cancer does get worse.You can choose to come off the study at any time without needing to give a reason.

What will happen to me if I take part?

If you decide to take part in this study, you will be asked to sign a consent form and will be given a copy to keep, along with a copy of this patient information sheet. Your study doctor/nurse will then check your medical records to determine if you can take part. Clinical information about your cancer history will be recorded and archival tissue from your cancer will be used.

If you are able to take part, you will continue to have appointments and monitoring of blood samples while on PARP inhibition treatment with your doctor/nurse. Every 3-4 months, an additional blood sample will be collected for the study and clinical information about your cancer will be recorded during the study. On one occasion we will also take a blood sample for storage. This is because we may identify mutations in genes that you inherited from your parents that might have caused your cancer to develop. If this happens, we would want to send a sample for a confirmatory test in a clinical (rather than research) laboratory.

If your cancer does not get worse during the study, your participation will continue until the end of the study.

If your cancer gets worse during treatment with a PARP inhibitor, you will be asked to attend for a tumour biopsy and a blood sample. The location of the biopsy will depend on the area

where your tumour has progressed. The biopsy may be performed under image guidance (ultrasound or CT scanning). Your doctor will discuss with you what the best treatment option is if your cancer has progressed. Some patients who have progression of their cancer on a PARP inhibitor may have surgery to resect the progressing tumour. Your doctor will discuss with you if this is appropriate in your case. If you are going to have surgery, then you would not need a biopsy for the study since we would be able to request for tissue to be taken for the study at the time of your operation instead. Clinical information about your cancer will be recorded for the study.

At consultation 6 months later your study doctor/nurse will collect further information about your cancer and cancer treatments. This visit can be performed virtually or via clinic attendance.

What elements of the study are additional to standard care?

The biopsy and additional blood samples taken in the study are not required for your standard treatment. The blood samples for the study will be taken at the same time as blood samples required for standard care.

What elements of standard care may I not receive if I agree to take part in this study?

Participation in this study will have no impact on your standard care. Your doctor/nurse will give you PARP inhibitor treatment for as long as they think it is helping you.

Clinic attendance

For your PARP inhibitor treatment, your doctor/nurse will need to have a consultation and monitor your blood tests regularly. This normally occurs monthly to begin with and then can be less frequent as you are established on your PARP inhibitor dose. Many cancer centres are performing some of these visits over the phone or video (virtually) with blood samples taken at your GP surgery or a local blood sampling service. The blood samples for the study will need to be taken in your cancer centre so 3-4 monthly your routine bloods will be taken at a face to face consultation in your cancer centre, and the study bloods will be taken at the same time. Participation in the study is likely to make your clinic appointment around 30 minutes longer.

Your biopsy visit may take several hours because depending on where the biopsy is taken from, you may need to be observed after the biopsy for around 4 hours. As your biopsy visit is additional to standard of care, travel expenses will be paid for this visit.

The 6 month post biopsy follow up visit can happen virtually or at a clinic attendance.

What are the possible disadvantages and risks of taking part?

If you participate in the study you will have a tumour biopsy or provide a tumour sample when having a surgical procedure. If having a biopsy, then you may suffer from side-effects. In

general you may have bruising, pain and/or infection at the biopsy site. In order to minimise pain, local anaesthetic may be given prior to the biopsy procedure and pain killers may be prescribed afterwards. If you develop an infection you may require treatment with antibiotics. The risk of infection is estimated to be less than 1 in 100. In very rare cases, biopsy associated bleeding may require a blood transfusion and/or intervention (radiological or surgical). Other adverse events due to a biopsy will depend on the location the biopsy is taken from. For example, if a lung biopsy is undertaken there would be a risk of pneumothorax (air around the outside of the lung which can sometimes cause shortness of breath). If CT guidance is used, there is a risk of allergic reaction to the contrast given to a patient before the CT, to achieve good quality images. In rare cases, patients can suffer from renal impairment as a result of contrast. This CT would be extra to those that you would have if you did not take part in this study. This procedure uses ionising radiation to form images of your body to aid biopsy. 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.

What are the possible benefits of taking part?

There will be no direct medical benefits to you from taking part in this study. Women diagnosed with ovarian cancer in the future will benefit from increased understanding of sensitivity and resistance to PARP inhibitors. This increased understanding should allow us to spare women who are unlikely to benefit from PARP inhibitor therapy, from the side-effects of a PARP inhibitor. It will also allow us to develop alternative treatments for those unlikely to benefit from PARP inhibition and for those who develop resistance to PARP inhibitors.

PART 2 – SUPPORTING / FURTHER INFORMATION

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak with the study doctor or nurse who will do their best to answer your questions.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence, then you may have grounds for a legal action for compensation but you may have to pay your legal costs. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism will still be available to you. If you do have a complaint, then please contact *(Insert local complaint department details here including contact name, number and address prior to printing patient information sheet on local headed paper)*.

Will my taking part in the study be kept confidential?

NHS Greater Glasgow and Clyde (NHS GG&C) 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. NHS GG&C will keep identifiable information about you for 15 years after the study has finished.

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
http://www.crukctuglasgow.org/eng.php?pid=privacy

You can be assured that any data collected during the course of this study and any of the results published will not identify you personally. Your medical records will only be available to the study doctors, your hospital consultant, responsible individuals from the Cancer Research UK Clinical Trials Unit (CTU), Glasgow and the study Sponsor. Information about you may also be looked at by personnel from Wellbeing of Women and/or Artios Pharma Limited as they are funding this study. The purpose of this would be to check that the study is being carried out correctly.

We will inform your general practitioner (GP) of your participation in this study. The information that will be exchanged includes details of your diagnosis, an overview of the study, the expected side effects of collecting blood samples and taking a tumour biopsy, and any update on your progress. Contact details will be given to your GP if he/she has any questions or concerns about the study or if he/she has any concerns if you were to become unwell.

The CRUK CTU (Glasgow), which is co-ordinating the study, will collect your initials, date of birth, sex at birth, and NHS number or Community Health Index (CHI) number at the time you are registered on to the study. This information will be stored securely and will be kept strictly confidential, with access provided only to authorised personnel who are performing analysis for the study.

Your consent for participation in this study also includes your consent to allow the use of the data in your medical/clinical record to be used for the purposes of future cancer research. Your consent also includes allowing these data to be linked to data coming from other sources such as cancer registries and medical clinical records. All data (personal, clinical, economic, and data coming from research on biological material) collected on your behalf will be treated in compliance with the European and UK applicable laws to ensure your confidentiality is maintained.

What will happen to any samples I give?

You will also be asked to consent to provide additional blood samples that will be used specifically for research purposes. Additional blood samples would be up to 50 millilitres (ten teaspoonfuls) and would be taken at your clinic visits.

You will also be asked to consent for the research team to collect archived tumour tissue that was taken originally to diagnose your cancer or removed at the time of an operation and was not needed for your routine diagnosis.

You will also be asked to consent for the research team to collect a tumour biopsy sample if your cancer gets worse during treatment with a PARP inhibitor. If you have surgery to resect a tumour that is increasing in size, the tumour sample for the study can be taken from the surgical specimen and no additional biopsy is required.

All samples (blood and tumour) will be sent to a laboratory here in the UK (Western General Hospital, Edinburgh) initially but could be sent to labs worldwide for downstream analysis. These samples will not contain any information that would identify you. With your permission, they may be used for other ethically approved and relevant investigations that would be conducted by qualified researchers in academic or commercial organisations (in the UK, or worldwide).

The analysis of the samples will involve examination of the genetic make up (DNA) of your tumour and also of your blood sample. As such, it is possible that during sample analysis we could identify an abnormality that has implications for the cancer risk of your relatives (known as a germ-line genetic aberration). In ovarian cancer, it is standard of care across most cancer centers for patients to have a blood sample tested for abnormalities in a panel of genes. Many ovarian cancer patients will therefore already be aware that they have a germ-line genetic aberration (10-20%) and be known to clinical genetic services who assist with assessing cancer risk of relatives and the need for genetic testing for relatives. In case we do identify an aberration that is not already known about, we will store some DNA so that the abnormality can be confirmed in a clinical grade lab and referral to clinical genetics can be made so that you and your family receive the required information to fully understand what the finding means.

You can choose to not be informed of any aberrations that you have inherited. This would also mean that we would not tell any member of your family.

It is unlikely that we will complete the tests on your blood and tumour samples for some time after they have been taken: it may take up to 4 years for all the tests to be performed on all the samples.

What will happen to the results of the study?

When the study ends, the results will be analysed and presented at national and international scientific and medical conferences before being published in a medical journal. The results

will also be published on the Cancer Research UK website. The confidentiality of all patients will be maintained. You will not be personally identified in any reports or publications resulting from the study. If you would like to obtain a copy of the published results, please check the Cancer Research UK website or ask your study doctor.

Who is organising and funding this research?

The study is being sponsored by NHS Greater Glasgow and Clyde, and is being co-ordinated by the Cancer Research UK Clinical Trials Unit (Glasgow), which is based at the Beatson West of Scotland Cancer Centre in Glasgow. Financial support will be provided by Wellbeing of Women and Artios Pharma Limited.

None of the doctors or other staff conducting the research are being paid directly for recruiting patients into the study.

How have patients and public been involved in this study?

We have engaged with volunteers from the Ovarian Cancer Action Research Network. They are involved in reviewing the study from development and will be involved throughout as the study progresses as part of the Trial Management Group.

Who has reviewed this study?

This study has been reviewed by a number of medical specialists during its development including the NCRI Ovarian Cancer Subgroup Committee and Wellbeing of Women. The study has also been reviewed and approved by the Sponsor's Research and Innovation Department and the Health Research Authority (HRA) Research Ethics Service [West of Scotland Research Ethics Committee (5)] to confirm that the study respects patients' rights and the protection of patients' health.

Contact for further information

If you have further questions about your illness or about clinical studies, please discuss them with your study doctor.

If you would like independent advice of further information you may also find it useful to contact:

Macmillan Cancer Support, an independent patient advisory group (freephone 0808 808 0000); website http://www.macmillan.org.uk, Head Office Address: Macmillan Cancer Support, 89 Albert Embankment, London, SE1 7UQ

Cancerhelp UK (Cancer Research UK), who provide a wide range of information for people with cancer: Freephone: 0808 800 4040, and website: www.cancerhelp.org.uk.

Alternatively you can contact Ovarian Cancer Action: Freephone **0300 456 4700,** website www.ovarian.org.uk **and** address: 8-12 Camden High St, London NW1 0JH.

If during the course of the study you have any questions regarding your participation or would like further study specific information before making your decision please contact:

Doctor:

Name Insert *local details*

Telephone Number *Insert local details*

Research Nurse:

Name Insert *local details*

Telephone Number *Insert local details*

24-Hour / out of hours contact: *Insert local details*

If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor or nurse.

Thank you for taking the time to read this information sheet. If you wish to take part you will be given a copy of this information sheet and a signed consent form to keep.

(Form to be on hospital headed paper)

CONSENT FORM FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

Patient Identification Number for this study:

(to be obtained post registration/randomisation)

Title of Project:

PAIRS: PARP Inhibitor Resistance Study (PAIRS) COHORT A

IRAS ID: 297051

	Please initial box
1. I confirm that I have read and understand the patient information sheet Version 1.1, 4th November 2021 for the above study, that I fully understand what is involved in taking part in this study, and that I have had the opportunity to ask questions.	☐
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 that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from the Cancer Research UK Clinical Trials Unit (Glasgow), the study Sponsor, the NHS organisation, and personnel from Wellbeing of Women and/or Artios Pharma Limited where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐
4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
5. I agree to the information detailed in the information sheet to be collected as part of the study.	☐
6. I understand that a letter and information regarding my participation in this study will be sent to my GP.	☐

7. I agree to take part in the above study. ☐

8. I give my permission to give extra samples of blood for research purposes and to be kept for future research as described in the information sheet for the above study. I understand how the samples will be collected, that giving samples is voluntary, and that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected. ☐

9. I give my permission for the research team to collect a tumour biopsy sample for research purposes and to be kept for future research as described in the information sheet for the above study. I understand how the samples will be collected, that giving samples is voluntary, and that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected. ☐

10. I give my permission for samples from the stored tumour tissue that was removed during my operation and was not needed for routine diagnosis and treatment to be collected and used for future research purposes as described in the information sheet for the above study. I understand how the tissue sample will be collected, that giving samples is voluntary, and that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected. ☐

Please initial

OPTIONAL

	YES	NO
1. I agree to give permission for data collected relating to me to be used for "Cancer Research" purposes as described in this information sheet including allowing this data to be linked to data coming from other sources such as cancer registries and medical records. I understand giving consent to the use of this data as described is optional and not mandatory for participating in this study.	☐	☐
2. I wish to be informed of any inherited mutations found during this research project and consent to confirmatory testing if appropriate. If you or your family wish to be referred to the Clinical Genetics Service this can be arranged through your doctor.	☐	☐
3. In the event that I am no longer alive, I wish my next-of-kin to be informed of any inherited mutations found during this research project	☐	☐

***Please sign and date below**:*

Name of Patient	Date	Signature

Name of Person taking consent	Date	Signature

When completed, 1 original for researcher; 1 original or photocopy for patient; 1 original or photocopy to be kept with hospital notes