(To be printed on local hospital headed paper)

TOPARP Part B

Trial of Olaparib in Patients with Advanced Castration Resistant Prostate Cancer.

PART B PRE-SCREENING PATIENT INFORMATION SHEET

TOPARP: Trial of Olaparib in Patients with Advanced Castration Resistant Prostate Cancer

We are inviting you to be pre-screened for a clinical study

- Before you decide whether to take part, 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. Discuss it with friends and relatives if you wish. Take time to decide if you wish to take part.
- You are free to decide if you want to take part in this research study. If you choose not to take part, this will not affect the care you get from your own doctors in any way.
- You can decide to stop taking part in the study at any time without giving a reason.
- Ask your study doctor if anything is not clear or if you would like more information.

Important things that you need to know

- You are being invited to be pre-screened for the TOPARP study to determine if you qualify for the main part of the study
- To qualify, your cancer cells must have one or more switches in specific genes we think may predispose to benefit from olaparib, the drug that will be tested in the main study
- Scientists know that olaparib has important anti-tumour activity against many but not all advanced prostate cancers
- We will test some of your tumour tissue taken at the time of your intial diagnosis of prostate cancer or at another timepoint prior to commencing the study in addition to saliva, to show what type of cancer you have; if you have the type of cancer that we think may be more suitable for olaparib treatment, then you will be invited to take part in the main part of the study
- We will also ask if you consent to your samples being stored for possible future research
- Additionally, we will ask if you give consent for genetic testing on your samples and if you would like to receive the results of this which may be relevant for the management of your cancer.

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How to contact us

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

1 Why are we doing this study?

The main aims of this clinical trial

i) To confirm whether a new drug called olaparib is effective against advanced prostate cancer
ii) To confirm if a particular group of patients are more suitable for olaparib treatment than others

What alternative treatments are there?

Taking part in pre-screening does not prevent you from receiving other study's drugs or any other treatment(s). If you are currently receiving a treatment against your cancer, consenting for pre-screening will not have any implication on your current treatment.

If you are found not to be eligible for the main part of the study or if at any time you are not able to, or do not wish to participate in this study, your study doctor will discuss other options with you.

Please also note that the trial may complete recruitment target and close to new patients whilst you are being pre-screened. If this happens, you will not be able to enter the trial but your study doctor will discuss other treatment options with you.

2 Why am I being asked to take part?

You have been invited to be pre-screened for a clinical study because you have been diagnosed with advanced prostate cancer. If this pre-screening shows that you may qualify, your doctor may offer you the option to participate in the main study. In that case, you will still need to have additional tests to check if you fulfil all the safety requirements. We will be inviting patients with advanced prostate cancer from hospitals across the UK to be pre-screened until we reach approximately 100 patients treated with olaparib in the main study.

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

Olaparib belongs to a class of drugs called Poly (ADP-ribose) polymerase (PARP) inhibitors, which are currently in clinical development for different types of cancer. This drug has been extensively tested in the laboratory and the clinic and has fulfilled the necessary safety and quality evaluation needed before government regulatory agencies allow the drug to be given to patients in a clinical trial. More than 2100 (Oct 2013) patients with a variety of cancers have been treated with olaparib, either on its own or in combination with other anti-cancer drugs. The regulatory agencies are continuing to assess the research and test results in detail from on-going clinical trials in a range of different cancer types. Olaparib is approved in Europe by the European Medicines Agency (EMA), and North America by the Food and Drug Administration (FDA), for the treatment of ovarian cancers.

The cells of the body contain DNA, which is the genetic material that contains the inherited information that makes us who we are. The DNA in cancer cells is damaged, this damage can be repaired by chemicals in the cell such as a protein called 'PARP-1'. Olaparib is known as a PARP-1 inhibitor because it stops PARP-1 from working. Blocking PARP-1 means the DNA in cancer cells cannot be repaired, which causes these cancer cells to die. In laboratory experiments, olaparib has antitumour activity against a wide range of cancers.

Some cancer cells rely more heavily on PARP-1 to repair any damage to DNA, whereas in normal cells there are alternative ways

whereby the damage can be repaired. Because of this it is thought that olaparib could specifically target cancer cells, helping to slow the progress of your disease with less effect on normal tissue. To date, olaparib has been shown to be a useful anticancer treatment in some ovarian, breast and prostate cancers with inherited defects in DNA repair. Scientists believe that there is a larger group of prostate cancer patients who may also benefit from this treatment.

4 What will I need to do if I take part?

Once you have read this information sheet, if you agree to take part in this study, you will be asked to sign a consent form before any study related procedures are performed. You will be asked to donate some of the tumour tissue that was taken as a biopsy or at surgery, when you were first diagnosed with prostate cancer or at any time prior to this study. This tissue will be used to test for cancers that are thought to be more suitable for treatment with olaparib. The tissue is usually stored in a laboratory at your hospital, but might need to be requested from departments outside your hospital.

If there is no tissue available, your doctor will discuss with you the need for a further tissue biopsy. To help us analyse this tumour tissue we will also take some normal DNA from your saliva.

Your donated samples will be sent to specialist laboratories at The Institute of Cancer Research to test for the type of prostate cancer you have. Specific tests that have already been established in the first part of this study will be evaluated in your donated tissue sample. Once the samples arrive at the laboratories, the results of the tests will take approximately two to three weeks. In a few cases, when the samples are very old or do not contain enough tumour, the laboratory might not be able to test the tissue and will ask your doctor whether another sample is stored at your hospital. It might then take longer to obtain a test result for you, but your doctor will be able to inform you if this is the case. If no additional tissue is available, your doctor will discuss with you the need for a further tissue biopsy.

The results will then be sent to your doctor who will tell you if you will be eligible for this study. These results may not benefit you in any way and are being done for research purposes to understand who is more suitable for olaparib treatment. If you are found to be eligible for the main study, your doctor will then inform you in more detail about the required procedures, risks and potential benefits and you will be then able to make a final decision about whether you want to participate in the main study by signing a specific consent form if you wish to take part.

Checks and Tests

Accepting to be prescreened for this study will not require any further hospital visits (unless you require a fresh tissue biopsy as described in the next paragraph) until you agree to participate in the main part of the trial, if your tumour is found to be of the type that could be sensitive to olaparib.

If you have not previously had a histological diagnosis, or if there is no archival tumour tissue to perform these tests, you will need to have another small biopsy of your tumour. Although taking these biopsies is routine for many cancers, we emphasise that in your case it will assist us in understanding the cause of this disease and to predict the likely benefit from olaparib treatment. The biopsy may also be used to inform future management of your

cancer through the results of tumour DNA testing. A sample (biopsy) of cancer tissue will be obtained and this is usually done as a day case. Your doctor will explain to you where he/she plans to take this sample from, the technique that will be used, and potential side effects.

All patients being pre-screened will be asked to donate a saliva sample and for some basic information such as name, age (date of birth), race and ethnicity. You will also be asked to give information about your current and past medical history, including your cancer, other illnesses and treatments you have taken in the past or are currently taking. The doctor will also ask you about how able you are to do day-to-day activities and care for yourself (performance status).

5 What are the possible benefits and disadvantages of taking part?

What are the possible benefits of taking part in this pre-screening study?

We hope that you will be helped by taking part in this study, but we can't guarantee this. The main objective is to test if you qualify for the main part of the study.

What are the possible disadvantages and risks of taking part in this study?

If there is no tumor tissue available to perform the pre-screening tests, your doctor will discuss with you about performing a new tumor biopsy.

Possible risks, discomforts or inconveniences associated with the collection of biopsies will depend upon the type of biopsy performed.

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

If you hold private medical insurance, you should check with the company issuing the insurance before agreeing to take part in this clinical study, as you will need to ensure that your taking part in the study will not affect the insurance.

6 Samples and genetic tests

What samples will I be asked to donate?

We ask that all patients donate some of their initial tumour tissue, which was taken at the time of diagnosis or at another time point prior to starting the study. If no sample is available for testing, we may ask you to undergo a new biopsy to obtain a cancer sample for the tests. We will also ask for a sample of your saliva.

Genetic analysis performed in research samples

We cannot guarantee giving you the results of these genomic tests due to unpredictable variability in sample quality. Rarely, the results of these genomic analyses may provide us with information that could potentially be relevant for your treatment, or indicate that your family members may have a higher risk of getting cancer or another disease. If this arises, your doctors will refer you (and your family if indicated) to an appropriate doctor with genetic expertise. You have a choice about how much

information you wish to receive about the results of these tests since they could potentially impact you and your family. You can indicate that you choose not to be made aware of these results in the consent form that you sign for this trial. Since you are participating in a cancer trial, however, we will always tell you about any results that may have a "direct impact" on the clinical management of your cancer. Please feel free to ask any questions and discuss your preferences with the study team members.

What will happen to samples I give?

Any samples you donate will be used to help us understand why people develop prostate cancer and how they react to treatment with olaparib. If we can show why some patients react to their treatment differently, this knowledge could help many patients in the future.

The group of medical professionals overseeing the TOPARP trial will also oversee the sample collection. Your tumour tissue may be labelled with your initials and hospital pathology number 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 your tumour's biological details to be compared to the treatment findings.
The tumour samples will be stored securely at The Institute of Cancer Research Laboratory.

Surplus archival tumour and biopsy material will be stored at The Institute of Cancer Research Laboratory indefinitely and in some cases returned to the local laboratories after the study is complete, depending on local practice. You are being asked to give permission for possible future research using these samples. The confidential nature of the tissue and associated data will be fully protected, and any other research using your tissue will first be reviewed and approved by an ethics committee.

7 More information about taking part

Do I have to take part in the pre-screening study?

No, your participation in pre-screening is voluntary. It is up to you to decide whether or not you wish to take part. Even if you refuse to participate, you will not be disadvantaged in any way and your future medical treatment will not be affected. If you do decide to take part you will be given this patient information sheet and a 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.

Likewise, the doctor conducting the study (the "study doctor") may ask you to stop pre-screening for Part B of the main study if:

- The results of certain tests show that you are not eligible for the main study
- You get any new health problems during pre-screening
- The study doctor thinks it is in your best interest to stop

Will my GP be involved?

Yes, your GP will be notified about your participation in this study. By signing the consent form you are agreeing to this.

Who is organising and funding the study?

The research trial is being carried out by a network of doctors across the UK. The trial is co-ordinated by The Institute of Cancer Research. The research trial is approved and funded by Cancer Research UK with laboratory support from Movember, Prostate

Cancer UK and Stand Up to Cancer. AstraZeneca, the company who manufacture olaparib, are supplying the drug free of charge and providing additional funding to support the management of the trial.

Your doctor will not receive any payments for including you in this research trial.

Who has reviewed the TOPARP study?

The trial has been approved by Cancer Research UK's Clinical Trials Awards and Advisory Committee, The National Institute for Health Research, one of the UK National Research Ethics Committees and the UK Regulatory Agency (Medicines and Healthcare Regulatory Agency, MHRA).

What will happen to information about me collected during the study?

Your medical notes will need to be seen by authorised members of the research team at your hospital, so that they can collect information needed for the TOPARP trial, and also to check that this information is correct. Your name, date of birth, post code and NHS number (CHI number in Scotland) will be passed to the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the study is being coordinated when you join the trial so that they can find you again if you lose touch with your hospital in the future.

Information from your medical records about your treatment and disease will be sent to the Trials Office on specially designed forms. You will be given a unique trial registration number when you join the trial which will be used together with your initials and date of birth, on all the forms / information that are sent to the Trials Office. All information about you will be treated as strictly confidential and nothing that might identify you will be revealed to any third party.

Representatives from the ICR-CTSU, the NHS Trust relevant to your taking part in research, the MHRA and ethics committee approving the trial and AstraZeneca (the pharmaceutical company that manufacture and supply olaparib) 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.

By signing the consent form you agree to access to your original medical records as outlined above.

We would like to be able to combine the medical information we collect about patients in this trial with information collected as part of other studies. In the future this will be a critically important way to advance our knowledge about prostate cancer and its treatment. If this happens, the completely anonymized information about you may be passed to other researchers, but they would not be able to identify you from the information provided.

What will happen to the results of the TOPARP study?

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 prostate cancer 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 new information becomes available during the course of the study?

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.

What if something goes wrong?

If you have any concerns 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. 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).

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.

8 Contacts 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.

Macmillan Cancer Support is 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) prostate cancer (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).

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/**). Other useful websites on prostate cancer treatment and trials are the Prostate Cancer UK and Prostate Cancer Foundation websites:
http://prostatecanceruk.org
http://www.pcf.org

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