(To be printed on local headed paper)

SOPRANO

Stereotactic Radiotherapy Alone or Followed by Niraparib for Oligometastases or Oligoprogression in Ovarian Cancer following PARP Inhibitor Therapy

PATIENT INFORMATION SHEET

Version 1.1 17th October 2023

INVITATION TO TAKE PART IN A CLINICAL TRIAL

We would like to invite you to take part in a clinical trial called SOPRANO.

Before you decide if you would like to take part it is important that you understand why the research is being done and what it will involve for you if you take part. One of your doctors or nurses will go through this information leaflet with you and answer any questions you may have or explain anything you don't understand.

Please take the time to read the information carefully and discuss it with your family, friends and your GP if you wish.

It is entirely up to you whether you want to take part or not. If you decide not to take part this will not affect the care you receive from your own doctors in any way.

SOPRANO is a phase II clinical trial to assess whether a certain type of radiotherapy called **stereotactic body radiotherapy (SBRT)** which targets radiotherapy very precisely at cancer cells, either on its own or followed by **niraparib**, a type of drug called a PARP inhibitor, may help increase the length of time before patients with some forms of advanced ovarian cancer need to start a different treatment such as chemotherapy. For the purposes of the SOPRANO trial, the term 'ovarian cancer' includes ovarian, fallopian tube and primary peritoneal cancer.

This information sheet contains information about the trial, why we are running it and what we hope to find out, as well as information about what it will involve for you if you decide to take part.

Please read Part 1 of this leaflet fully. If you are interested in the trial and wish to find out more then please continue to read Part 2 before making your decision to take part in this trial. A glossary can be found at the end of this leaflet, which may help you when reading the information.

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If you have any questions about this trial please talk to your doctor or nurse:

<local name and contact number>

PART 1- About the SOPRANO trial

1. What is the purpose of the trial?

SOPRANO is looking at a treatment called **stereotactic body radiotherapy (SBRT)**. We want to see whether the use of this treatment increases the time until patients require further treatment for their cancer.

SOPRANO is also looking at a drug called niraparib. Niraparib is a type of targeted therapy drug called a PARP inhibitor. PARPs are proteins that help damaged cells repair themselves. Niraparib blocks (inhibits) how PARP proteins work in cancer cells. Without PARP proteins, these cancer cells become too damaged to survive and they die. We want to see whether the use of this drug can help increase the amount of time a patient benefits from SBRT.

Niraparib is currently approved for use as a maintenance treatment for patients with early or relapsed ovarian, fallopian tube or primary peritoneal cancer who have completed chemotherapy treatment and achieved a good response.

2. What is Stereotactic Body Radiotherapy (SBRT)?

Radiotherapy involves the use of targeted beams of high energy X-rays to kill cancer cells. Radiotherapy cannot tell the difference between cancer cells and normal cells and your medical team carefully plans the treatment so that only the cancer and as few normal cells as possible receive the highest dose of radiotherapy.

SBRT is a way of targeting radiotherapy very precisely to the cancer using lots of beams at different angles to ensure that a very high radiation dose is given to the cancer and as low a dose as possible is given to surrounding healthy tissues.

3. Why am I being invited to take part?

You are being invited to take part because:

- You have previously been treated with PARP inhibitor therapy (e.g. olaparib, niraparib or rucaparib), but now some of the cancer cells have stopped responding to the PARP inhibitor therapy and your cancer has progressed.
- Your cancer has only progressed at a small number of sites (3 or less at any one time). This is called **oligo-metastatic (OMD)** or **oligo-progressive disease (OPD).**

SOPRANO will look to see if treatment with SBRT either on its own or followed by niraparib, may help increase the length of time before patients with some forms of advanced ovarian cancer need to start a different treatment such as chemotherapy where your doctor thinks this is safe to do so.

4. Do I have to take part?

No, you do not have to take part; it is up to you to decide. If you do want to take part you will be asked to sign a consent form and you will be free to withdraw at any time, without giving a reason if you don't want to. This will not affect the standard of the care you receive. Your doctor will discuss alternative treatment with you and offer you the most suitable treatment available.

5. What will happen if I decide to take part?

If you decide you would like to take part in the SOPRANO trial, we will give you this information leaflet to keep and you will need to sign a consent form to record your agreement to participate. Before you are able to take part, you will need to undergo some tests. Most of these are routine but others are needed to check that it is safe for you to take part and that the trial is right for you.

These assessments will only be carried out after you have provided your consent to take part. They may all be performed in one visit or over a number of visits, and your doctor or nurse will discuss this with you in more detail.

These assessments and tests will include:

- Medical history and detailing any current medications you are taking
- Physical examination including blood pressure (BP), heart rate, height and weight
- Blood tests to confirm you are able to undergo SBRT safely
- A pregnancy test for all women able to get pregnant
- CT, MRI or PET scan

The following tests may also be needed depending on where in your body your ovarian cancer has progressed:

- If your cancer has progressed in the liver **–** blood tests will be carried out to find out how your liver is functioning and whether there is any existing liver damage. Your kidney function will also be looked at to make sure this is working well before any SBRT treatment is given.
- If your cancer has progressed in an **adrenal gland** – blood tests will be carried out to check the adrenal gland is functioning and your kidneys are working well.
- If your cancer has progressed in the **lung** – lung function tests will be carried out.
- If your cancer has progressed in a **spinal bone** - an MRI of the whole spine will be carried out. More information about what is involved in an MRI scan is provided below.
- ***DMSA scan***

  Depending on where your cancer has progressed, it may mean your kidneys will receive a high dose of radiation during the SBRT treatment. It is important to find out if your kidneys are functioning properly before delivery of any SBRT. To do this a scan called a

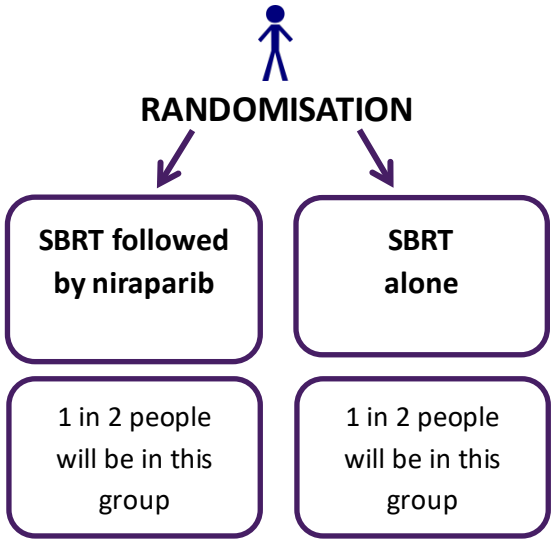
DMSA scan, which stands for dimercaptosuccinic acid (DMSA), may be performed depending on your hospital's standard practice. Not everyone will receive this type of scan and your doctor or nurse will discuss this in more detail with you if required.

Further details about the types of scans you may receive in this trial can be found in the Imaging Section on page 13 of this information leaflet.

Trial Treatment Allocation

Once all the tests are complete and it is confirmed that you are able to take part in the trial, the treatment you will receive will be decided. This will not be decided by you or your doctor or any other person. The choice is made at the time you enter the trial and is made at random by a computer. This process is called **randomisation** and it is the best way to make sure that the participants in each treatment group are as similar as possible. If one group does better than another group it is more likely to be because of the treatment and not because participants in one group are somehow different from those in the other group.

In SOPRANO, for every **ONE** participant randomised to the SBRT followed by niraparib group **ONE** participant will be randomised to the SBRT alone group.



All participants will receive SBRT and those participants randomised to the SBRT followed by niraparib group will commence treatment with niraparib 4 weeks after completion of SBRT and will continue to receive niraparib until their doctor thinks they should stop niraparib and change to a different treatment.

Whichever treatment group you are randomised to, everybody who takes part in the trial will receive the best possible care and regular monitoring by the local clinical care team.

Trial Assessments

Participants in both groups will need to come back for a clinic visit 4 weeks after completion of SBRT so that the research team can find out how you are and participants in the SBRT followed by niraparib group can commence niraparib. After this you will need to return to clinic 8 weeks after randomisation, and every 8

weeks for the first year and then every 12 weeks thereafter.

At these visits the following assessments will be performed:

- Physical examination and routine blood tests.
- Toxicity assessment to find out if you are having any adverse reactions to the treatment you are receiving.
- Tumour imaging assessment to check the status of your disease. The types of scans you have at your follow up visits will depend on your hospital's standard practice. In most cases this will be either a CT scan or a PET/CT scan, but could involve different types of scan depending on where your cancer has progressed. Scans will be required every 8 weeks for the first year and every 12 weeks for the second year. Thereafter scan frequency will be as recommended by your local research team.
- Collection of blood and stool samples for research.

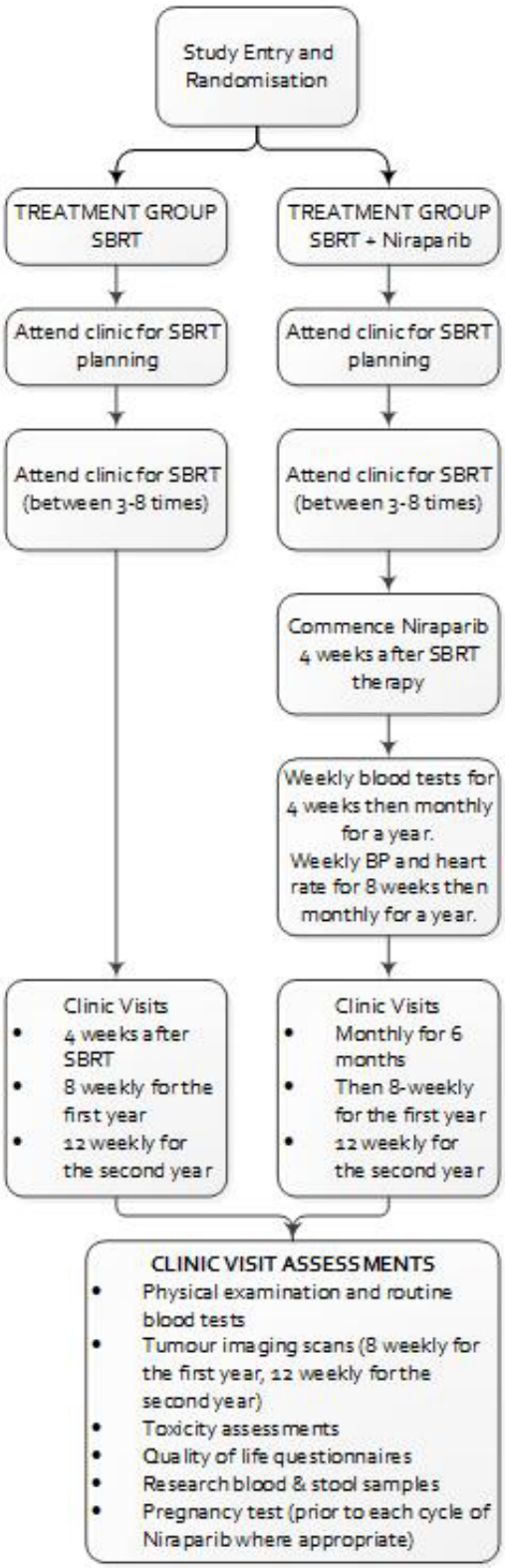
If you are randomised to the SBRT followed by niraparib treatment group you will attend clinic monthly for 6 months to collect a supply of niraparib treatment and then 2 monthly if your local research team are happy with your progress. You will also require an additional blood test weekly for the first 4 weeks following the start of niraparib and then monthly for the first year. Blood pressure and heart rate will also be monitored weekly for 8 weeks following the start of niraparib and then monthly for the first year.

These assessments can be performed locally by your GP practice if they do not coincide with scheduled hospital visits and if your GP practice is able to offer this service. Blood pressure and heart rate assessments may also be carried out at home if you have access to a blood pressure monitor. We will ask you to keep a record of these assessments and report them to your local trial team.

You will continue to attend regular clinic visits until your doctor thinks you should stop your PARP inhibitor therapy and change to a different treatment.

After this the research team will collect information on how you are doing and what treatments you are receiving but you will not undergo any further SOPRANO trial assessments.

This flow chart shows the visit time points and assessments to be conducted as part of the SOPRANO trial:



6. What will happen during SBRT & niraparib treatment?

What do I have to do before my SBRT treatment?

To confirm SBRT is a suitable treatment for you, a group of clinicians called a Multi-disciplinary Team (MDT) will review your scan results. Members of the MDT will include the clinicians at your hospital, the SOPRANO clinical team at the Royal Marsden Hospital and the SOPRANO trial team at the Institute of Cancer Research who are part of the trial team. In order to do this, the research team at your hospital will upload your scan images onto a central portal where they can be reviewed and discussed by all members of the MDT.

Your SBRT treatment is designed specifically for you and has to be carefully planned by your cancer specialist and other specialised staff at the hospital (radiographers, physicists). For some participants 'markers' will need to be placed within or around the tumour. The markers, called fiducial markers, show up clearly on X-rays and CT scans, and help clinicians to see exactly where the cancer is located. Inserting the markers is very similar to having a biopsy and it will allow us to give treatment very accurately. Your doctor will tell you if you need this procedure before your SBRT. More information about these markers is provided in Section 8 'Fiducial marker side-effects'.

Before you receive SBRT you will need to have a radiotherapy planning scan. This

will take place at the Radiotherapy department and will take about 30 minutes. It will involve a CT scan being taken of the sites to be treated and you may in some instances also have an MRI scan depending on where your cancer has progressed. These procedures will allow measurements to be taken that are needed for planning the treatment, including the location of the tumour and the normal organs and tissue surrounding it. It is important that the position you lie in during your planning scan is the same position you are in when having your SBRT as this will help to make sure that clinicians are treating the cancer cells very accurately at each treatment. In some circumstances you may be given an immobilisation device to use and your doctor will provide information on this.

To ensure that the SBRT treatment delivered in the trial is safe and the same for all participants taking part in the trial the National Radiotherapy Trials Quality Assurance (RTTQA) team will look at the planning scans for all participants in the trial. This will involve the research team at your hospital uploading the scans to a central, digital 'platform'. All data that is uploaded to the RTTQA platform will have all patient identifiable information removed before it leaves your hospital and will be labelled with your unique Trial ID.

Access to the RTTQA platform is restricted so only people working on the SOPRANO trial and the administration team working on the RTTQA platform will have access to your information. We ask that you initial the consent form to show that we have your permission to do this.

The QA team that will review your scans will be made up of members of the SOPRANO trial team and members of the RTTQA team. To ensure that the treatment being planned is safe, the team will need to know if you have received any prior radiotherapy treatment as this will affect whether the trial SBRT can be delivered safely or not.

So along with your scans, information about any previous radiotherapy treatment you have received will also be uploaded to the QA platform. This information will be pseudo-anonymised so that no one will be able to identify you from this. We would ask that you initial the consent form to say that we have your permission to do this.

What do I have to do during my SBRT treatment?

The number of treatments or fractions you will need will depend on where the lesion being treated is located. You can expect to receive treatment every other day or every day. The average length of treatment will be 3 treatments given over 5 days. However, you could receive up to 8 treatments given over 19 days. Your doctor will discuss your treatment programme with you.

Your radiotherapy treatment will be similar to having an X-ray and you will not feel anything. The length of time each treatment will take will depend on the type of machine used at your hospital:

- A **Linac** (Linear Accelerator) machine will deliver the treatment over a few minutes but you will need to lie still for about 20 – 30 minutes whilst the machine moves around the body to deliver the radiotherapy.
- A **Cyberknife®** (robotic radiosurgery system) machine will take longer, usually 45-60 minutes but in some cases may take up to an hour and a half (90 minutes).

Once you have completed your treatment you will see your hospital doctor or nurse who will assess how you are feeling and if you are experiencing any side effects from the treatment. After this visit you will be seen regularly for SBRT follow up at 4 and 8 weeks after the end of your SBRT treatment and then at 8 weekly intervals for the first year, and 12 weekly intervals for the second year as per your usual standard care.

What are the possible side effects of SBRT treatment?

Patients who have SBRT treatment can experience some side effects. No one can predict whether you will experience any side effects and how minor or severe they may be. They are usually mild but can sometimes be more serious. The possible side effects will depend on which part of your body is being treated. You are unlikely to experience side-effects outside the site that was treated with SBRT.

Acute side effects (first few weeks):

- Tiredness
- Shortness of breath and dry cough
- Nausea and / or vomiting
- Temporary worsening of original symptoms
- Skin changes at treated sites
- Hair loss (temporary/permanent)*
- Diarrhoea
- Swallowing problems / pain on swallowing*

**Not all side effects listed will be relevant to your specific treatment with SBRT and some side effects will be relative to the area treated with SBRT.*

Late side effects (months to years):

- Skin changes at treated sites
- Bone fracture
- Chest wall pain / rib fracture
- Reduction in breathing capacity
- Liver impairment
- Kidney impairment
- Small risk of serious bleeding
- Small risk of late swallowing problems
- Small risk of damage to the gut
- Small risk of damage to heart function
- Small risk of nerve damage
- Small risk of spinal cord injury

What will happen during niraparib treatment?

If you are randomised to receive SBRT followed by niraparib, you will start to take niraparib at the visit 4 weeks after completion of your SBRT treatment. Niraparib is an oral tablet. Your dose will depend on your weight and blood test results and should be taken once daily with water. Subsequent supplies of Niraparib will be provided monthly for 6 months and then 8-weekly if your local research team are happy with your progress.

What are the possible side effects of niraparib treatment?

Very common side effects (more than 1 in 10 in 100 patients):

- Decrease in the number of blood platelets (thrombocytopenia) that help blood to clot
- Decrease in the number of red blood cells (anaemia) that carry oxygen
- Decrease in the number of white blood cells (leukopenia) that fight infection
- Decrease in the number of neutrophils (neutropenia), a type of white blood cells (leukocytes) that fight infection
- High blood pressure (hypertension)
- Feeling like your heart is skipping beats or beating harder than usual (palpitations)
- Painful and frequent urination (urinary tract infection)
- Shortness of breath (dyspnoea)
- Runny or stuffy nose (nasopharyngitis)
- Cough
- Headache
- Dizziness
- Feeling weak (asthenia)
- Lack of energy (fatigue)
- Difficulty in sleeping (insomnia)
- Joint pain (arthralgia)
- Back pain
- Stomach pain (abdominal pain)
- Indigestion (dyspepsia)
- Feeling sick (nausea)
- Vomiting
- Frequent watery stools (diarrhoea)
- Difficulty passing stool (constipation)
- Decreased appetite

Common side effects (up to 1 in 10 in 100 patients):

- Infection due to low white blood cell counts (neutropenic infection)
- Low blood cell counts due to a problem in the bone marrow or blood cancer starting from the bone marrow (Myelodysplastic Syndrome [MDS]/Acute Myeloid Leukemia [AML])
- An irritation or infection in the tubes that carry air in and out of the lungs, that causes a cough (bronchitis)
- Fast heartbeat (tachycardia)
- Swelling of lower legs and feet (peripheral oedema)
- Muscle pain (myalgia)
- Rash
- Decrease in weight
- Feelings of sadness, depressed (depression)
- Feelings of worry, nervousness or unease (anxiety)
- Impaired concentration, understanding, memory and thinking (cognitive impairment)
- Inflammation of the eye (conjunctivitis)
- Nosebleed (epistaxis)
- Sore, red mouth (stomatitis)
- Swelling or irritation of the lining of the mouth, throat, oesophagus, stomach or

intestines (mucosal inflammation/mucositis)
- Abnormal taste in mouth (dysgeusia)
- Dry mouth
- Increased sensitivity of the skin to sunlight (photosensitivity)
- Decrease in potassium in the blood (hypokalaemia)
- Increased level of creatinine in your blood (blood creatinine increase), which may be a sign of kidney damage
- Increased levels of substances in the blood produced by the liver, which may be a sign of liver injury (aspartate aminotransferase [AST] increased, alanine aminotransferase [ALT] increased, gamma-glutamyl transferase [GGT] increased)
- Other abnormal labs (alkaline phosphatase [ALP] increased)
- Allergic reaction (hypersensitivity, including anaphylaxis).

Uncommon side effects (up to 1 in 100 patients):

- Fever with low white blood cell count (febrile neutropenia)
- Severe life-threatening infection due to low white cell counts [associated with low blood pressure and possible organ failure (for example, heart, kidney and/or liver), (neutropenic sepsis)]
- Decrease in number of all types of blood cells (pancytopenia)
- Confusion (confusional state/disorientation)
- Seeing or hearing things that are not really there (hallucination)
- Inflammation of the lungs which can cause shortness of breath and difficulty breathing (non-infectious pneumonitis)

Rare but potentially serious side effects (up to 1 in 1000 patients):

- Severe increase in blood pressure (hypertensive crisis)
- A brain condition with symptoms including seizures, headache, confusion, and changes in vision (posterior reversible encephalopathy syndrome [PRES])

Secondary Primary Malignancy:

PARP inhibitors may also cause a new primary cancer (that is, a cancer other than the one for which you have been treated). In 2 studies comparing niraparib to placebo (sugar pill), new primary cancers were observed in a small number of patients who took niraparib and was similar to those in patients who took placebo.

Safe Handling:

Wash your hands after handling the trial drug. If a caregiver is giving the trial drug to you, he or she should wear disposable gloves. Notify your trial doctor if it appears that the trial drug is damaged or defective in any way.

If you experience any side effects or feel unwell then you should contact your local trial doctor as soon as possible to let them know.

7. Will I be asked to do anything else?

Quality of Life Questionnaires

One of the reasons we are carrying out the SOPRANO trial is to see if participants have any side effects from SBRT or niraparib

therapy. We would like participants in both treatment groups to complete Quality of Life questionnaires to describe any side effects that you may experience.

We will ask you to complete a total of 6 questionnaires, the first before the start of SBRT, another 4 weeks after completion of SBRT and then at approximately 4, 6 and 12 months after trial entry, with the last being at your end of trial visit if your disease progresses. Each questionnaire should take no longer than 20 minutes to complete.

You will be given your questionnaires in clinic. When completed the questionnaires should be handed to your hospital team who will forward them to the SOPRANO trial team at the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the trial is being coordinated. The answers you give to the questions are for the SOPRANO trial only and will be treated in the strictest confidence. This means your hospital will not know how you have answered, so if you are having any problems you still need to tell your doctor.

A member of your medical team will explain the questionnaire and answer any questions that you have. Some of the questions may seem to be a bit repetitive but these are standard questionnaires and we would ask you to answer them as best you can.

Tissue Collection

We will ask you to donate blood, stool and tumour tissue samples which we will use as part of the trial to find out more about the effects of SBRT and niraparib.

Blood Samples - We ask that all patients who take part in the trial consent to the collection of blood samples. Approximately 8 teaspoons (40ml) of blood will be taken at the start of the trial and 4 teaspoons (20ml) of blood will be taken 4 weeks after completion of SBRT, at then again at 16, 24 and 48 weeks after trial entry. If your cancer progresses we would take another 4 teaspoons (20ml) of blood at that point as well.

Stool Samples - We also ask you to provide samples of your poo. A sample will be required at the start of the trial, 4 weeks after completion of SBRT, at then again at 16, 24 and 48 weeks after trial entry. If your cancer progresses we would like another sample at that point as well. Instructions and tubes to collect these samples will be provided.

Tumour Samples – We require a sample of your tumour tissue. This will involve the use of **archival tissue** taken from the tumour sample which was used to confirm your cancer diagnosis or at another time point prior to starting the SOPRANO trial. This will already be stored in the pathology department of your local hospital and will not require any additional tissue to be taken from you.

Optional tumour samples - We would also like to ask for **fresh biopsies** from sites of further disease progression although we understand this is not always possible. This will be entirely optional and you will only be asked if your clinician thinks it is appropriate and your tumour is in a

suitable location to biopsy. If you don't want to donate fresh tumour tissue you can still take part in the SOPRANO trial.

Blood and tumour tissue samples will be analysed for potential changes in DNA (genetic changes). The results of these genetic tests will not be shared with your or your local research team.

8. How to decide whether to take part in the trial?

What are the possible benefits and disadvantages to taking part?

There is no guarantee that you as an individual will benefit directly from taking part in this trial. SBRT is given with the aim of shrinking cancer and/or delaying time to cancer worsening. The aim of SOPRANO is to find out whether SBRT is helpful in the treatment of your cancer and if treatment with SBRT either with or without Niraparib, may help increase the length of time before patients with some forms of advanced ovarian cancer need to start a different treatment such as chemotherapy, as this is not currently known. The information gained from this trial may help in the treatment of future patients with cancer similar to yours.

By taking part in this research trial you may need to visit the hospital more often than normal. 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. The trial organisers are unable to offer reimbursement of travel expenses.

During this trial, blood samples will be taken to perform a variety of tests, some for safety purposes and some specifically for research purposes. The number of blood tests required in this trial will be more than if you were not taking part in a research trial. Risks linked with blood sampling include pain from the needle being inserted, light headedness, possible fainting and (rarely) infection.

Where it is possible and you have agreed to the procedure, a biopsy may be taken from a new site of disease progression. CT guidance may be required to perform the biopsy. Possible risks, discomforts or inconvenience associated with the collection of biopsies will depend on the location and type of biopsy to be 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 trial doctor. The taking of biopsies may cause some pain, redness, swelling and slight bruising at the biopsy site. There is also a small risk of bleeding, infection and wound healing problems following your biopsy. For lesions within the lung, there is a small risk of lung puncture (pneumothorax) that may require a short hospital stay to treat. You will have the opportunity to discuss all the possible side effects and the type of biopsy your tumour will require with your trial doctor.

Imaging

More information about the types of scan you may receive as part of taking part in the SOPRANO trial is provided below. Not everyone will have all of these scans and this will depend on where your cancer has progressed and your hospital's usual practice. This can be discussed in more detail with your doctor or nurse.

CT Scan: CT stands for **computerised tomography** and this type of scan uses X-rays and a computer to create a detailed image of the inside of your body. You may have an injection of a contrast medium dye before the scan. This is a dye that shows up some body tissues more clearly and you have the injection through a small thin tube (cannula) in your arm. Before having the contrast dye your radiographer will ask you about any medical conditions or allergies as some people can be allergic.

MRI Scan: You may receive this type of scan to see if you have any cancer lesions in your brain or if your cancer has progressed in your spinal bones. MRI stands for **magnetic resonance imaging** and this type of scan uses magnetism and radio waves to build a picture of the inside of your body. When having an MRI scan you will be made as comfortable as possible before you start. You will be asked to remain still during the entire procedure. People who are afraid of enclosed spaces may feel anxious or nervous while in the scanner. Some people may also find it hard or painful to hold one position for more than a few minutes. If you have any concerns about having this type of scan you should discuss these with your doctor or nurse.

PET Scan: PET stands for **positron emission tomography** and this type of scan produces a detailed 3 dimensional (3D) image of the inside of your body. PET scans are often combined with CT scans (PET/CT) to produce even more detailed images. A PET scan involves you having a very small amount of radioactive material injected first. The amount of radiation is very small and does not make you feel unwell; it goes out of your body very quickly. Not everyone will need to have a PET/CT scan and this will depend on your hospital and whether they normally use these types of scans.

DMSA scans: DMSA stands for dimercaptosuccinic acid and a DMSA scan may be performed to find out if your kidneys are working properly before you receive any SBRT. This will involve a small amount of radioactive material being injected into a vein which allows the activity of the kidneys to be calculated. Not everyone who takes part in SOPRANO will need a DMSA scan and this will also depend on your local hospital and they type of scans they normally use.

The number and type of scans you receive by taking part in the SOPRANO trial may be different to what you would receive if you were not taking part in the trial. Patients receiving SBRT receive an additional CT scan which is the radiotherapy planning CT scan. You would not receive this scan as

part of your normal care if you were not taking part in this trial.

Long term risks associated with SBRT treatment, CT scans, X-rays or radioactive tracers

As a patient in this trial you will receive SBRT – a significant ionising radiation dose which wouldn't normally be considered part of the routine care for your cancer. Such ionising radiation can cause cell damage that may, after many years or decades, turn cancerous leading to another primary tumour. However, this radiotherapy is considered standard care for some other patients with similar cancers, and therefore the risks from the radiation dose associated with it may be considered to be similar as that for those other patients.

If you take part in this trial you will also have planning CT scans, verification scans done during the treatment sessions, and other follow-up CT or PET scans. Some of these scans will be extra to those that you would have if you did not take part. These scans also use ionising radiation, but in this instance to form images of your body and/or provide your doctor with other clinical information. The radiation dose from these scans will be extremely small compared to the dose from the SBRT treatment. Ionising radiation may cause cancer many years or decades after the exposure, but the chances of this happening to you as a consequence of these scans is insignificant compared to the risk from the SBRT treatment.

Fiducial marker side-effects

You may need the use of fiducial markers to help direct the SBRT and this will be discussed with you before your planning visit. The fiducial markers will need to be inserted before your radiotherapy planning scan. The insertion of fiducial markers is similar to having a biopsy and lasts approximately 10-15 minutes. If you experienced a lot of discomfort with previous biopsies your doctors may offer you sedation (or if necessary, general anaesthetic). Markers are inserted with a needle into or near the location of disease with local anaesthetic. This is usually through the skin. You can go home after your procedure. The markers do not interfere with your treatment. Your doctor may give you antibiotics to prevent infection.

For a few days afterwards you may also notice a small amount of discomfort. Please let your doctor or nurse know about any side effects that you are concerned about so they can advise you what to do. Their telephone numbers are at the end of this information leaflet. There is also 24-hour support available from your hospital to provide access to immediate medical care in the event of any serious problems.

Risks to an unborn child

There could be risks to an unborn child due to treatment given in this trial; therefore, if you are pregnant you cannot enter the trial. If you become pregnant during the trial, these risks could affect you or your unborn child. Before entering the trial,

during treatment with niraparib and at the end treatment with niraparib, pregnancy tests will be carried out for all women who are able to get pregnant. If applicable, you must agree to use highly effective birth control from entry into the trial and for 6 months after the last dose of trial treatment which you can discuss with your doctor.

If you think you may be pregnant, you must tell your 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 from your clinical team.

What are the alternatives for treatment?

You and your hospital doctor should have discussed the treatment options available to you. Make sure that you have discussed these with your doctor before deciding whether to take part in this trial or not.

This completes Part 1 of the Patient Information Sheet. If you are still interested in participating in the SOPRANO trial please read the additional information in Part 2 before making your decision.

Part 2 – General Information about the SOPRANO trial

1. Confidentiality

Who will have access to my data?

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

The Institute of Cancer Research's lawful basis for processing your information is for the performance of a task carried out in the public interest and it is necessary to process sensitive health and genetic information for the purposes of scientific research with appropriate safeguards in place to protect personal information, as required by the United Kingdom General Data Protection Regulation (UK 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 trial, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information 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 trial in accordance with our instructions.

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

Will my taking part in this study be kept confidential?

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

complete and 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 your direct care team 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 the registries 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 the pharmaceutical company GlaxoSmithKline which manufactures the trial drug 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 trial for at least 5 years after the trial has finished.

Will information about me be shared with other researchers?

When you agree to take part in a research trial, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations now or in the future. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

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

2. Blood and tissue sample information

What will happen to any samples I donate?

In the SOPRANO trial we ask that all participants consent to provide blood and stool samples for research and for us to request a sample of their initial tumour tissue, taken either at the time of diagnosis or at another time point prior to starting the trial, where this is available. We would also like to ask participants to consent to a fresh tumour biopsy if your cancer further progresses whilst in the trial. This is optional and will depend on whether it is possible to safely biopsy your progressing lesion. Details of the samples requested are described in Part 1 of this information leaflet. We would ask that you sign the appropriate part of the SOPRANO consent form if you agree to the collection of all or some of these samples. Consent for samples to be stored for future research is optional and can be withdrawn at any time.

The samples you donate will be used to help us better understand the effect of SBRT treatment and niraparib, identify better ways to monitor response to treatment and find out more about your cancer.

The group of medical professionals overseeing the SOPRANO trial will also oversee the sample collection. Your tumour tissue or blood and stool samples may be labelled with your Trial ID, initials and hospital pathology number when they are sent to the research lab. When they arrive at the laboratory they will be coded meaning that your personal details will be removed and replaced with a unique number. By doing this your confidentiality will be maintained whilst still allowing biological information to be compared to treatment findings.

The blood, stool and tumour samples will be stored securely at The Royal Marsden Hospital and/or The Institute of Cancer Research biobank facilities and it is intended that much of the analysis of these samples will happen here. But some of the samples may also be sent to other research institutes (which may be outside the UK) or companies approved by The Institute of Cancer Research for analysis. In all cases your confidentiality will be maintained.

Any tumour and/or biopsy material will be stored at the Royal Marsden Hospital and/or The Institute of Cancer Research laboratories indefinitely and in some cases returned to the local pathology laboratories once the trial is complete

depending on local practice. We ask for your permission for possible future research using these samples. This is optional you do not need to agree to this in order to participate in the trial. Where information from the samples and/or associated data could identify you, the information will be held securely with strict arrangements about who can access and use the information. Any other research using your tissue will first be reviewed and approved by an ethics committee.

3. General information about SOPRANO

What happens if I don't want to carry on with the trial?

Your participation is entirely voluntary. If you agree to take part and then change your mind later on you can withdraw from the trial at any time without giving a reason. If you withdraw from the trial it will not affect the standard of care you receive. Your doctor will discuss alternative treatment with you and offer you the most suitable treatment available.

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

If you lose capacity, you will remain in the trial. However, your trial treatment may be discontinued. This decision will be made by your treating clinician. If treatment is discontinued, follow up of your health status in the trial will continue.

What if there is a problem?

If you have any concerns about any aspects of the trial you should ask to speak with your trial doctor or nurse who will do their best to answer your questions. Their contact details can be found 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 NHS complaints mechanisms are available to you. Concerns should be raised by speaking to a member of staff at your hospital. We recommend that you obtain a copy of your hospital's complaints procedure or policy if you intend to make a complaint.

[Sites in England] Concerns can also be raised by talking to your local Patient Advice and Liaison Service (PALS). You can contact the PALS team at [insert Trust name] on [insert relevant contact details].

[Sites in Scotland] Concerns can also be raised by talking to the Patient Advice and Support Service (PASS). You can contact PASS via the National Citizens Advice Bureau on 0808 800 9060 or through your local Citizens Advice Bureau (www.cas.org.uk/patientadvice).

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 SOPRANO trial. We may also need to send this information to the ethics committee who approved the trial, the Medicines and Healthcare Products Regulatory Agency and all the doctors who are responsible for participants in this trial. 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.

What if I have private medical insurance?

If you have private medical insurance, please check with the company that your medical insurance policy will not be affected before agreeing to take part in this trial.

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 ovarian 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 relevant information becomes available?

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

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

What happens if I don't want to carry on with the trial?

You are free to withdraw from, or reduce your level of participation within SOPRANO at any time. You do not have to give a reason and your future treatment will not be affected by your decision. Your medical team will discuss your treatment options with you and will offer the most suitable treatment available.

If you were to reduce your participation, for example by stopping trial specific hospital visits, we would like to continue to collect information on your progress that is routinely recorded in your medical records. This is so that the overall quality of the trial is not impaired and enough information is collected to answer the main aim of the trial.

If you decide you want to stop participation and do not want any more information to be sent to the research centre, trial data collected before your decision will still be processed along with other data collected as part of the clinical trial, however no new data will be added to the trial database and you may request that all retained identifiable samples are destroyed to prevent future analysis.

Who is organising and funding the research?

The SOPRANO trial is being carried out by a network of doctors across the UK and the Chief Investigator is Professor Susana Banerjee of The Royal Marsden NHS Foundation Trust. The trial is coordinated by The Institute of Cancer Research Clinical Trial and Statistics Unit and funded by the pharmaceutical company GlaxoSmithKline (GSK). Your doctor will not receive any payments for including you in this research trial.

Who has reviewed the trial?

The trial has been approved by the joint Royal Marsden & Institute of Cancer Research Committee for Clinical Research on behalf of the Sponsor, The Institute of Cancer Research (ICR). The trial has also been approved by the London - Brighton & Sussex Research Ethics Committee.

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 local research team.

4. Further information

Who else can I contact for further information?

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

Macmillan Cancer Support is a registered charity providing information, emotional support and publications about all aspects of cancer for cancer patients and their families. You can contact one of their Cancer Information Nurse Specialists on the **Macmillan Support Line**: Freephone 0808 808 00 00 Monday to Friday 9:00am to 8:00pm. In addition to their nurses, the Macmillan Support Line also has other specialist teams that can provide advice and information relating to welfare benefits, financial issues and everyday practical concerns.

You can learn more about clinical trials on the Cancer Research UK and Be Part of Research websites:

- https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial
- https://bepartofresearch.nihr.ac.uk/

Thank you for your interest in our research

5. Glossary

Lesion – An area of abnormal tissue. A lesion may be benign (not cancer) or malignant (cancer)

Metastases – Cancer which has spread from the part of the body where it started to a different place in the body.

Mutation – A change to the DNA sequence that makes up a gene.

Oligometastases - Cancer which has spread to a small (1-3) number of places in the body.

Oligoprogression – Cancer which has either got bigger and/or spread to a small (1-3) number of places in the body.

PARP – a protein that helps damaged cells repair themselves.

PARP Inhibitors – a targeted therapy drug that blocks how PARP proteins work causing cancer cells to die.

Progression – Cancer which has either got bigger and/or spread to another place in the body.

Pseudo-anonymised – identifiable personal data replaced with a trial identification number.

Randomisation – A method used to randomly select a treatment group.

SBRT – **Stereotactic Body Radiotherapy** – a type of radiotherapy that specifically targets cancer cells.