Participant Information Sheet

OCTOVA:
Trial of different drug and treatment combinations for patients with inherited genetic changes who are considering further therapy to treat their ovarian cancer.

- You are being invited to take part in a clinical research study for patients who are considering further treatment for ovarian cancer and who have inherited genetic changes (a BRCA mutation).
- Before you decide, we would like you to understand why the research is being done and what it would involve for you.
- One of our team will go through the information sheet with you and answer any questions you have. You should talk to others about the study if you wish.
- Please ask us if there is anything that is not clear. This sheet is for you to keep and read in your own time.
- Participation in this study is entirely voluntary. If you decide not to take part, this will not affect your care in any way.

Why have I been invited?

- You have been invited to consider entering this study because you were diagnosed with a BRCA mutated ovarian cancer and you are not responding to the treatment that was already given to you(platinum drugs), and your doctors are considering a further therapy to treat your ovarian cancer.
- One hundred and thirty two patients like you will take part in this study, in 13 hospitals across the UK

Why is this study being done?

- We are always trying to find ways of improving treatment outcomes for ovarian cancer, a disease which affects around 7000 women every year in the UK. Sometimes inherited genetic changes mean that the cancer cells respond differently to certain therapies. This study will assess patients to see if their tumours will shrink in response to one of three possible treatments:

  a) Standard **chemotherapy (paclitaxel)**

  b) An oral treatment called **olaparib**

  c) A combination of **olaparib** and another oral agent, **cediranib.**

- **Paclitaxel** is a chemotherapy drug. It also known by its original brand name, Taxol. The drug is made from the needles of a particular type of yew tree. It works by stopping cancer cells separating into

two new cells, so it blocks the growth of the cancer. It is a standard treatment for various types of cancer, including ovarian cancer.

- Your body naturally produces a protein called PARP (Poly-(ADP-ribose)-polymerase). When the cancer cells in your body are damaged or injured by radiation and certain types of cancer drugs, PARP may help them to recover and then the treatments may not work so well. **Olaparib** is designed to stop the action of PARP. This may prevent the cancer cell from repairing itself and re-growing.
- **Olaparib** is approved for use in patients who have relapsed ovarian cancer that continues to respond to platinum-based chemotherapy (such as carboplatin or cisplatin). This study will test whether olaparib also works in patients with ovarian cancer that no longer responds to platinum drugs and who have inherited genetic changes (a BRCA mutation).
- For a cancer to grow, it needs its own blood supply to develop. **Cediranib** is a new type of drug that blocks cancer from developing its own blood supply, and this may help to slow or stop cancer growth. Cediranib is not yet approved for use in the UK and is considered experimental. Across the world, more than 5,800 patients have been treated with Cediranib in clinical trials.
- **Cediranib** and **Olaparib** work in different ways to have an anti-cancer effect. A recent study in patients whose ovarian cancer has recurred, has shown that the anti-cancer benefits of cediranib and olaparib are enhanced when these drugs are taken together.
- In this study we want to compare the effectiveness and tolerability of olaparib with standard chemotherapy. We also want to determine if the combination of cediranib and olaparib is more effective than olaparib alone, and whether there are any side effects of this combined treatment.

Do I have to take part?

- No, it is up to you to decide and participation in the study is entirely voluntary. You are free to withdraw from the study at any time and without giving a reason. This will not in any way affect any future care you receive from your medical and nursing team.

What are the alternatives for treatment?

- You do not have to take part in this research study to receive treatment for your condition. Your doctor will discuss all of the treatment options available to you, including any other relevant clinical trials. You will have the opportunity to consider all of this information and ask any questions you might have before making a decision.
- If you decide not to participate in the study, or are not suitable for the study, then you will receive standard care and your doctor will discuss this with you.
  Your doctor will review treatment options that are appropriate for you together with the potential risks and benefits of each treatment.

What would taking part involve?

- You will first be asked to attend a screening visit. At this visit your study doctor will review this information sheet with you and talk you through what will happen in the study. You will have the opportunity to ask questions and decide whether or not you wish to participate in this study. If you

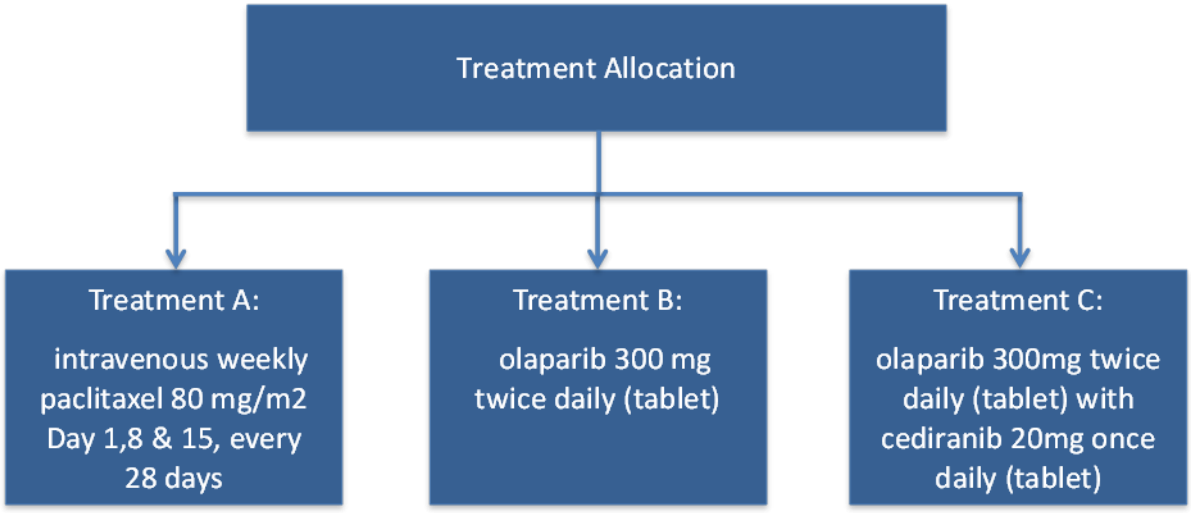
decide that you would like to take part, we will ask you to sign a consent form. You will be given a copy of that consent form to keep along with this information sheet.

- After you have signed the consent form you will undergo some tests and evaluations to determine if you are suitable for this study. These tests and evaluations are important to ensure that it is safe for you to be included in the study. These will include an ECG, measurement of your blood pressure, an echocardiogram (echo), CT or MRI scans and blood tests. Some of these procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them performed recently, they may not need to be repeated. This will be up to your study doctor.
- If the results of these screening tests are satisfactory we will then register you with the OCTOVA trial office in Oxford. The trials office will use a computer to randomly allocate you (like selecting one of three straws) to a specific treatment schedule – standard chemotherapy, olaparib tablet or olaparib and cediranib tablets.
- If you are allocated to a tablet treatment, you will be given a treatment diary card that will tell you what treatment you will have on each day and will help remind you when to take your tablets. We will ask you to complete this every time you take your medication, and bring it with you to each study visit.
- The total amount of time that you will remain on the study will depend on the study treatment you are allocated to, and the amount of benefit you gain from treatment and the types of side effects you may have.
- You will continue taking the study treatment(s) until your study doctor feels that they are no longer of benefit to you. This would be the case if scans show your cancer has worsened or if the side-effects of treatment are not tolerable and it is no longer safe for you to continue.
- If you are assigned to paclitaxel treatment and your disease worsens, you will be offered the opportunity to receive olaparib treatment instead.
- After receiving study drug for 18 months, your visits will be become less frequent and you will attend hospital clinics in line with standard of care. We will still want to collect details about any side effects you may experience and any admissions to hospital.
- If your cancer worsens or you choose to stop treatment on the study, then you will be asked to attend a final visit. If you are still taking the study drugs at the time of the decision to stop, you will be asked to attend for an additional visit 28 days after your last dose of study drug.

What would happen to me during the study?

Treatment

You will be randomly allocated to one of the treatment schedules:



Clinic visits - During your treatment you will have to attend the following visits:

- Treatment month 1**: Clinic visits once a week**
- Treatment month 2 and 3: **Clinic visits every two weeks**
- After three months: **Clinic visits every four weeks**

If you are unwell or develop side-effects you will be able to contact your research nurse **at any time** and come into the clinic for earlier review. You may also have additional visits just before each treatment cycle to check your blood results and also for CT or MRI scans (see below). In this study, one treatment cycle lasts 28 days.

At Every clinic Visit, you will be asked about:

- Any change in the medications you are taking;
- Any problems you are having;
- Any side effects that you are experiencing, which may or may not be related to the study;
- Whether you have made any visits to other doctors or hospitals.

- We will be checking you closely for any side-effects to the treatment. If the side-effects are troublesome, your study doctor will either reduce the dose or stop the medication for a short period or permanently.

During a study visit, you will also have some or all of the following tests (summarised in the Table at the end of this Information Sheet):

General health checks

- Physical examination and disease assessment
- blood pressure and heart rate,
- Height, weight and body surface area
- Performance status – doctor will assess your ability to perform daily tasks

- Urine sample
- Pregnancy test (unless you are unable to have children)
- TSH/T4 blood test to check levels of your thyroid stimulating hormone

CT (Computed Tomography) or MRI (Magnetic Resonance Imaging) Scans

- You will have several CT or MRI scans as part of this study. This is to assess whether your disease has changed as a result of your treatment. You may have already had many of these scans as part of your routine care. CT or MRI scans will be performed by radiographers (people trained in carrying out imaging investigations).
- You doctor will decide, in line with the hospital practice, whether you will have a CT or MRI.
- MRI stands for magnetic resonance imaging. This type of scan uses magnetism and radio waves to build up a picture of the inside of the body. MRI is completely painless, but the scanner is very noisy. An MRI scan can take anything from 30 minutes to an hour and a half.
- CT scan (or CAT scan) stands for computerised (axial) tomography scan. This means a scan that takes a series of X-rays and uses a computer to put them together. The scan is painless. The CT machine takes pictures of your body from different angles and gives a series of cross sections (slices) through the part of the body being scanned. A very detailed picture of the inside of the body can be built up in this way. The scan itself only takes about 10 to 15 minutes, but you will need some preparation time beforehand and should expect to be in the hospital for up to a couple of hours.
- A CT or MRI scan will measure the status of your disease at the following time points:
  - Baseline (within 28 days prior to 1st dose of study treatment)
  - Then every 8 weeks
  - End of treatment visit
- If you finish your treatment early because of the side effects but your disease has not worsened you will continue to have a CT or MRI every 8 weeks.

Echocardiogram

- An echocardiogram (echo) is a scan which gives a detailed view of the structure of your heart, and which can show how well your heart is working. It is a painless test that takes roughly 30-45 minutes and will be done by a cardiologist or a sonographer (a technician trained to do ultrasounds).
- You will have one echo during the screening period if you have previously received treatment that might have affected your heart or you have mild heart disease. This test will be performed to make sure that your heart is in a good shape and that it is safe for you to receive our study drugs.
- If you are assigned to the treatment C (olaparib and cediranib) and have previously received treatment that might have affected your heart or you have mild heart disease, you will have one echo every 3 months once you start your study treatment.

Electrocardiogram

- An electrocardiogram (ECG) checks how well your heart is working. Small sticky pads that are attached to wires are put on your chest, and your heart beat can be seen as an electrical trace on a computer screen.
- You will have one ECG within 7 days before you start treatment to monitor your heart function. This test allows your doctor to assess whether you are well enough for the OCTOVA study treatment.
- If your doctor thinks it is in your best interest, you may have an additional ECG during treatment.

Routine Blood Samples

- You will have blood samples taken to monitor your blood count, kidney function, liver function etc. These blood tests are part of normal clinical care. These standard blood tests will be analysed by the hospital where you are having treatment.
- A varying amount of blood will be taken from a vein (usually your arm) at each visit (please see the table at the end of this information sheet for the approximate amounts).
- Routine bloods can be taken up to 72 hours before the visit and at a local center that your study doctor has confirmed is acceptable to take and report the results. Sometimes, your study doctor might need to repeat a blood test to confirm a result or if the first test failed for some reason. Your study doctor may also carry out other blood tests as part of your local standard of care.

CA-125 Biomarker Blood Samples

- CA-125 is a protein produced by some ovarian cancers and is known as a tumour marker for ovarian cancer. A tumour marker is a chemical given off by cancer cells that circulates in the bloodstream, so it can be measured with a blood test. This test helps us to measure if the treatment you are being given as part of this study is working. You would have had these tests even if you were not taking part in this study, however it may not have been so often.
- A blood sample will be taken (approximately 1 tablespoon) to measure CA-125 levels at the following time points:
    - Baseline (within -14 days of 1st dose)
    - On day 1 of each treatment cycle (every 28 days)
    - End of treatment visit
- If you finish your treatment early because of the side effects but your disease has not worsened you will continue to have CA-125 blood tests every 8 weeks.

Research Tissue and Blood Samples

- As well as looking to see how good these drugs are at killing cancer, we will also ask your permission to use the sample of cancer (biopsy) that was taken when you were diagnosed, as well as to take samples of your blood during the study. If some women benefit from the treatment, or have side effects when others do not, these samples could help us to understand why. This is called 'biomarker' research.
- A biomarker is a substance, measured in blood or tissue that may reflect the severity or presence of a disease. The biomarkers may consist of genetic material (coded information that is stored in the

form of DNA and RNA molecules and that provides the instructions to make our bodies work), proteins or parts of proteins (the molecules that carry out the instructions and are the functional units of all cells) or metabolites (the by-products of working cells). The information gained from this research may be used in the development of new therapies and diagnostic tests.

- A blood sample will be taken (approximately 1.5 tablespoon) for biomarker research at the following time points:
  - Baseline (within 14 days of 1st dose)
  - Before treatment on day 1 of cycle 1
  - Before treatment on day 1 of cycle 2
  - Before treatment on day 1 of cycle 3
  - End of treatment visit

Ascites (swollen tummy)

- Cancer can sometimes make fluid build up in your tummy (abdomen). The medical name for this is ascites. Your doctor can put a small tube into the abdomen to drain off the fluid. This reduces the swelling and makes you feel more comfortable.
- Ascites will only be drained off if this is in your best interest and it would be done in line with the standard of care, not this study. However if you develop ascites, we would like to collect a small sample of a drained fluid, and test whether it contains cancer cells. This will also help us to assess your response to the study treatment.

Additional Research: Quality of Life

- As part of the study we would like to know how you feel both physically and emotionally. To collect this information you will be asked to complete 'Quality of Life' questionnaires at regular intervals. This will be before you start treatment, then at the start of each treatment cycle, and then at the end of treatment. The questionnaires should take less than 15 minutes to complete. These questionnaires will remain confidential at all times.

Will any genetics tests be done?

- All the cells in your body contain DNA which encodes the genetic information that produces individual proteins to help cells function.
- Tests will be performed on your blood and tumour samples to look for changes in DNA that may alter the likelihood of tumour cells responding to study treatment. The samples will only be marked with study number assigned to you, rather than your name or other information that could identify you. Your identity will not be known to any other researchers.

What will happen to any samples that I give?

- Your routine blood samples will be sent to the local hospital laboratory for tests to help identify and manage any side effects during the study. These will be reported to the study doctor according to normal hospital practice.
- The research blood samples will be processed, frozen and stored in your local hospital laboratory until a batch shipment is organised for them to be sent to the research laboratory for testing.
- Your archival tissue samples will be sent to the research laboratory straight away.
- We will ask your permission to store these specimens so that we are able to repeat any tests on them if necessary. We will also ask your permission to store any surplus material to use for possible other tests in the future. Any further use of surplus blood or tissue samples after this study has concluded would be carried out under separate ethical approval.
- With your consent, any surplus blood and tumour sample at the end of the study will be sent to a research biobank. A biobank is like library where researchers store samples they may use in future research. The samples are kept with some details of your medical history, but not your personal details.
- All your samples will be stored securely and confidentially using a study number that will be assigned to you, rather than your name or other information that could identify you. Your identity will not be known to any other researchers.
- The OCTOVA trial management group will not make any financial gain from the research blood and tissue samples that you agree to give.

What do I have to do?

- You must tell your study doctor and/or research staff about all past and present diseases and allergies of which you are aware, and all medications which you are currently taking. While you are in the study, if you feel the need to take other medications, including over-the-counter medications or alternative therapies, please talk with your research nurse or doctor before you take them.
- We will give you a small card that gives details of the study and contact numbers, should you need any advice. In case of an emergency, the card will inform the doctors that you are on a clinical trial and let them know the drugs you are being treated with. You will need to carry this card with you at all times and show it to any doctors treating you, so they have details of your treatment.
- It is important you attend all your clinic appointments. The study staff may contact you by phone to remind you about your next visit, and to see how you are feeling.
- You should report any side effects to your local research team (study doctor or nurse), who can prescribe medicines that usually control them.
- If you are having any problems with side effects, we would always recommend you get in touch with your local research team (study doctor or nurse). Contact details are given at the end of this Patient Information Sheet.
- If you have private medical insurance, please inform your insurance company before agreeing to take part in the study.

What should I consider?

Regular medications

- Before you begin the study treatment it may be necessary to change or stop some of your regular medications. The doctor will discuss any changes with you in advance.

Other cancer medication

- During your participation on study, you will not be given any other cancer treatment (other than study treatment) for your disease.

Pregnancy and breastfeeding

- If you are pregnant or breastfeeding you cannot take part in this study. This is to protect the developing baby from the potential harm of the study medication. If you are sexually active, we would like to discuss appropriate means of contraception when you agree to take part in the study. Two forms of appropriate contraception should be used from signing the consent form until 6 months after stopping treatment.
- Acceptable methods of contraception include: combined (oestrogen and progesterone containing oral, intravaginal or transdermal) or progesterone only (oral, injectable or implantable) hormonal contraception associated with inhibition of ovulation, intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion, vasectomised partner (provided that partner is the sole sexual partner of the woman of child bearing potential and that the vasectomised partner has received medical assessment of the surgical success) and true sexual abstinence where this is in line with your preferred and usual lifestyle.
- If you become pregnant while receiving study medication or within 6 months after taking your last dose of study medication, you must tell the study doctor right away. If this happens, study medication will be discontinued. The study doctor will follow you and your pregnancy to birth.

Clinic visits

- You may have to visit the hospital more than you would if you did not participate in this study. Your study doctor will also collect more information from you than they would normally; this is in order for us to understand how the study drug(s) work and whether they make a difference to your treatment.

Food and Drug Interactions

The blood levels of medication you will be taking in this study can be affected by certain foods and medications, so they should be avoided. These include: grapefruit, grapefruit juice, Seville oranges, star fruit, pomegranate, verapamil, ketoconazole, rifampin, phenytoin, fluconazole, ciprofloxacin, erythromycin, St. John's wort and modafanil. Be sure to tell your healthcare provider about all medications and supplements you take.

Will I be reimbursed for taking part?

- You will not be paid for taking part in this study. However, your local hospital may be able to reimburse your travel expenses as per their local policies. You should discuss with your study nurse before you start the study whether they will be able to refund additional travel expenses.

What are the possible benefits of taking part?

- We cannot promise the study will help you but we hope the information we get from this study will help improve the treatment of women with advanced ovarian cancer.
- Cediranib and olaparib are new treatment options and can only be used within clinical trials at present in women with platinum resistant ovarian cancer (i.e. ovarian cancer that is no longer benefitting from cisplatin or carboplatin). Although Cediranib is unlicensed and not part of standard care, there is evidence from previous clinical trials that when given with olaparib it improves control of disease.

What are the possible disadvantages and risks of taking part?

- You will be having a few additional scans that you would not ordinarily have.
- The CT scans are associated with exposure to a small amount of radiation. The extra radiation dose that you will receive from the research scans in this study is less than the background radiation you will have been exposed to during 73 years of living in the UK. This can also be understood as an additional lifetime risk of cancer induction from all the CT scans in the trial of approximately 1 in 100 or ~ 1%. It is important to understand that risks relating to cancer induction may not be expressed for many years, and are therefore of reduced significance in some patient groups, e.g. those where life expectancy is reduced, or the elderly. In some such groups the cancer induction risk is unlikely to be expressed during the remaining years of life. This is considered unlikely to impact upon your health.
- If your study doctor has decided that you will have an MRI scan, rather than a CT scan, the study may involve more MRI scans than normal. MRI scans for most people are not considered uncomfortable; however some patients can find them claustrophobic.
- As part of the study you will also have more blood tests and one extra ECG than you would have undergone if you were not participating in the study. While the ECG test is painless, removal of the sensors can produce mild discomfort similar to removing a plaster and some people may develop a mild skin reaction to the sensors.
- You will also have a series of blood samples taken, which will require a needle or cannula to be inserted into a vein in your arm. This may cause pain, bruising or bleeding, however the blood samples will be taken by trained staff, and the volume taken will be minimal, please refer to the table at the end of this sheet for approximate amounts

- The treatment used on this study can cause side effects. Some people have very few side effects, while others may experience more. The side effects described here won't affect everyone having the treatments given in this study.

Paclitaxel side effects	
Very Common (affects more than 1 in 10 patients)	• Joint or muscle weakness, pain, aching or loss of sensation in the limbs. These usually reduce or disappear several months after stopping treatment with paclitaxel • Infection – usually of the urinary tract or upper respiratory tract. This may be associated with low blood cell count resulting from receiving Paclitaxel. This can sometimes be fatal. • Bone marrow suppression, which can lead to decreased blood cell counts and may result in infections, anaemia with paleness and weakness, and bruising and bleeding • Low blood pressure which may cause you to feel light-headed, particularly when standing up • Pain in the muscle or joints • Hair loss • Nausea and vomiting • Mild diarrhoea • Soreness of the mouth or tongue • Mild allergic reactions including flushing and skin rash • Nerve problems – these may appear as pins and needles in the hands and feet
Common (affects 1 to 10 in 100 patients)	• Temporary mild nail change and skin changes, reactions at injection sites (localised swelling, pain, and redness of the skin) • A slowing of the heart rate (a slow pulse is not harmful; however if you should develop any other irregularities in heart rate during treatment, an ECG and other tests may be required) • Injection site reactions (local swelling, pain, redness, hardening of tissues, death of skin tissue, extravasation (leaking of drug outside the vein) resulting in cellulitis (painful swelling and redness) • Temporary mild changes to the nails and skin
Uncommon (affects 1 to 10 in 1000 patients)	• Increases in liver function tests that indicate your liver may not be working properly; changes in liver function can sometimes be severe • Irregular heartbeats • Fainting • High blood pressure (may give you headaches) • Yellowing of whites of eyes and skin

Paclitaxel side effects	
	• Pain in the middle of your chest which may be caused by heart disease • Pain or weakness in heart muscles (heart muscle degeneration) • Irregular heartbeat (may be caused by irregular impulse conduction)
Rare (affects 1 to 10 in 10,000 patients)	• Pneumonia • Effect on nerves that control the muscles, resulting in muscle weakness in arms and legs (motor neuropathy) • Itching, skin rash/redness • Accumulation of fluid in the whole body (oedema) • Dehydration • Loss of energy • Problems with your lungs such as inflammation or accumulation of fluids, which may make it difficult to breathe • Abdominal pain caused by inflammation in your bowel, bowel obstruction or perforation of the wall of your bowel • Inflammation of your pancreas (pancreatitis) • Heart failure • A feeling of discomfort or uneasiness
Very rare side effects (less than 1 in 10,000 patients)	• Increased frequency of heartbeat • Nettle rash (urticaria) • Effect on the brain (encephalopathy) • Damage to the liver which may be severe (hepatic necrosis). This may have an effect on brain function (hepatic encephalopathy). This can sometimes be fatal. • Loss of hearing or ringing in the ears • Balance problems • Visual disturbances • Staggering when walking • Dizziness • Headache • Constipation • Abdominal pain which may be caused by accumulation of fluid in the abdomen (ascites), inflammation in your gut or blood clot in the blood vessels to your bowel • Loss of appetite • Confusion • Shock • Loosening of finger or toe nails (you are advised to wear protection on your hands and feet when exposed to the sun)

Paclitaxel side effects	
	• Heartburn, nausea and/or vomiting which may be caused by inflammation of the gullet • Cough • Muscle weakness, cramps, severe bowel or abdominal pain or dizziness when standing up which may be caused by a disease of the nervous system • Acute leukaemia (blood cancer) or related condition (myelodysplastic syndrome) which your doctor will check for
Not known (Frequency cannot be estimated from the available data)	• A condition called tumour lysis syndrome which may cause high levels of sodium or potassium or low levels of calcium in your blood • A swelling of part of the back of your eye (macular oedema) • Visual disturbances such as seeing flashes of light (photopsia) or floaters • Disease of your connective tissue (scleroderma) • An autoimmune disorder that may affect your skin, joints, kidneys, brain, and other organs (systemic lupus erythematosus)

Olaparib side effects	
Very common (affects more than 1 in 10 patients)	• Nausea or vomiting • Fatigue • Anaemia • Diarrhoea. Your doctor may prescribe a medicine to treat this. If it gets severe, tell your doctor straight away. • Dyspepsia (heartburn) • Dizziness. If you feel dizzy, take special care when driving or using tools or machines. • Headache • Taste change • Loss of appetite • Decrease in number of white blood cells that support the immune system (lymphopenia) • Increase in blood creatinine (this may mean your kidneys are working less well)
Common (affects 1 to 10 in 100 patients)	• Sore mouth • Skin rash • Pain in upper stomach area (upper abdominal pain) • Reduced white cell count (leukopenia/neutropenia) • Reduced platelet count (thrombocytopenia)
Uncommon (affects 1	• Allergic reactions

to 10 in 1000 patients)	• Dermatitis • Pneumonitis (lung inflammation). If you experience any new or worsening symptoms of shortness of breath, you should contact your Study Doctor as soon as you can • Myelodysplastic syndrome and acute myeloid leukaemia (AML). Your Study Doctor will monitor your blood cell levels during the study and may decide you need to have further tests, which may include a bone marrow sample or a blood sample. o Myelodysplastic syndrome is a pre-cancerous condition where the bone marrow isn't as good at producing blood cells as it was before (red blood cells and/or white blood cells and/or platelets) o Acute myeloid leukaemia is a cancer of the bone marrow where many abnormal and immature white blood cells (blast cells) are made while normal functioning blood cells are not made.

Cediranib

Side effects caused by cediranib have been well recorded from patients in earlier studies. Cediranib has been used with chemotherapy in other cancer types, and is not thought to increase toxicities caused by chemotherapy

Cediranib side effects	
Common (affects 1 to 10 in 100 patients)	• Fatigue • Diarrhoea • High blood pressure • Protein in urine
Uncommon (affects 1 to 10 in 1000 patients)	• Nausea and vomiting • Muscle weakness • Sore mouth and/or throat • Dry mouth or hoarseness • Reduced platelet count • Reduced neutrophil count • Hand and foot syndrome • Proteinuria (protein in the urine) • Anorexia (loss of appetite) and weight loss • Headache • Changes in thyroid function • Bleeding and haemorrhage including bleeding in the tumour • Infections (minor)
Rare (affects 1 to 10 in 10,000 patients)	• Impaired liver function test • Stroke • Poor function of the heart, in some cases leading to the heart failing to pump adequately • Brain swelling caused by high blood pressure called reversible

Cediranib side effects	
	posterior leukoencephalopathy syndrome (RPLS). In rare cases it can cause death, however, it may be reversible if it is recognized and treated promptly. This usually involves a brain scan, treatment of blood pressure and discontinuation of any drugs that are suspected of causing it. The symptoms include high blood pressure, headache, seizures, vision problems or blindness, dizziness and confusion. If you develop any of these symptoms, you should contact your doctor or other healthcare professional immediately.

What happens when the research study stops?

- Once your involvement in the study has ended, your doctor will decide how your cancer will be managed from this point. Your doctor will discuss what is best with you. You may continue to receive study treatment as long as your doctor believes it is safe to do so or until your doctor consider that the treatment is not benefitting you.
- After this point you won't need to attend any further study visits. However, we will ask your doctor to contact the trial office periodically to confirm how you are.

What if there is a problem?

- Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed individually.
- The University of Oxford, as Sponsor of this study, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.
- If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact your study team (details at the end of this sheet) or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224, or the head of CTRG, email ctrg@admin.ox.ac.uk.
- The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team please go to the NHS Choices website: http://www.nhs.uk/pages/home.aspx, and search for PALS.
  <add local contact details here as required>

Will my participation in the study be kept confidential?

- Yes. We will follow ethical and legal practice and all information about you will be handled in confidence.
- Information collected about you during the study will be kept at the OCTOVA Trial Office, which is part of the University of Oxford. This information will include your initials and date of birth taken

from your medical notes, and is strictly confidential. Your study record will be identified by a unique study number and your personal identify will not be identifiable from this number.

- Responsible members of the University of Oxford or the NHS Trust where your treatment is based, as well as the UK regulatory agency the MHRA, may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations.
- The results of the study will be shared with the pharmaceutical company AstraZeneca (the drug manufacturer), and may also be shared with other groups in the UK and across the European Union. However, your data will only be referred to by a unique study number, and it will not be possible to identify you.
- Anonymised data may also be presented outside the European Union, and these areas may have fewer rules about data protection. The Sponsor will make every effort to ensure your anonymised data is adequately protected.
- Details about you, your treatment, any side-effects you have, how the disease responds and how you are during and following study treatment will be recorded in your medical notes at your hospital.

What if relevant new information becomes available?

- Data from this study will be monitored regularly by the trial Data and Safety Monitoring Committee. Sometimes we get new information about treatments being studied in trials. If this happens, you will be informed by your local research team and you will be given the opportunity to discuss it with them. If you decide to continue in the study, you may be asked to sign an updated consent form.
- In some circumstances your study doctor might consider it best for you to withdraw from the study. They will explain the reasons and arrange for your care to continue outside the study.
- If the study is stopped for any other reason, your study doctor will explain this to you and arrange for your continuing care.

What will happen if I don't want to carry on with the study?

- You are free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. The research team will respect your decision and we will happily answer any questions you might have at the time.
- You may choose to stop treatment and still remain on study follow-up. Alternatively, you may choose to leave the study completely.
- Research information and samples that have already been collected will still be used in the study. If you experienced any unwanted effects from the study treatment, we may need to collect further information about those effects from your medical record after you have withdrawn from the study.
- We will ask for your consent to do this.

Involvement of the General Practitioner/family doctor (GP)

- Your GP will be notified about your participation in this study. We will ask for your consent before we do this.

What will happen to the results of the study?

- The results of the study will be presented at national and international meetings. It is also our intention to publish the results in a medical journal.
- Studies such as this take many years to complete and for the final results to be available. If you wish to receive information on these results of this study, please ask your doctor.
- A printable results summary will be made available on the Cancer Research UK website.
- All results will be anonymous; it will not be possible to identify you in any report or publication.

Who is organising and funding the research?

- The study is being sponsored by the University of Oxford, who are legally responsible for the study organisation and for overseeing the work of the researchers. The trial is run by the Oncology Clinical Trials Office (OCTO).
- Financial support for this study is received from AstraZeneca, the manufacturer of cediranib and olaparib.
- The study is endorsed by Cancer Research UK and supported by the National Cancer Research Network (NCRN). Cancer Research UK and the NCRN receive money from the government, charities and industry.
- None of the doctors or other staff conducting the research are being directly paid for including and looking after patients in this study.

Who has reviewed the study?

- All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect the interests of any patients that may take part.
- This study has been reviewed and granted a favourable opinion by the London – Chelsea Research Ethics Committee. It has also been approved by the Health Research Authority, the Medicines and Healthcare Regulatory Agency (MHRA), the Research and Development Department at your hospital, and the Cancer Research UK Clinical Trials Advisory and Awards Committee (CTAAC).
- The study has also been reviewed by independent international experts, the Chemotherapy and Pharmacy Advisory Service (CPAS), Patients Active in Research (Thames Valley) and AstraZeneca.

Who are the researchers?

- The Chief Investigator, responsible for leading and directing this study is Dr Shibani Nicum, Consultant in Medical Oncology at the Oxford University Hospitals NHS Foundation Trust.

Thank You

Thank you for considering taking part in this study and for taking the time to read this Patient Information Sheet, which is yours to keep.

If you decide to take part in the study, you will be asked to sign a consent form. You will be given a copy of your signed consent form to keep.

Sources of Further Information and contact details

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

Local site contacts

Please discuss any questions you may have with your study doctor or members of the research team:	
Your study doctor is:	
Name:	Contact phone number:
Your research/specialist nurse is:	
Name:	Contact phone number:

If you or your relatives have any other questions about your disease, or about being involved in a research study, you may wish to contact one of the following organisations that are independent of the hospital at which you are being treated:

- **Macmillan Cancer Support** provides practical, medical and financial support and work towards the improving cancer care. They can be contacted at:
  Tel: 0808 808 00 00 (freephone)
  Or visit their website at: http://www.macmillan.org.uk/
- **Cancerhelp** (Cancer Research UK) who provide all aspects of information for people with cancer. Their contact details are:
  Tel: 0808 800 4040 (freephone)
  Or visit their website at: http://cancerhelp.cancerresearchuk.org/
- **Ovacome -** A registered charity providing support and information for all those affected by ovarian cancer.
  Tel: 0845 371 0554
  Or visit their website at: www.ovacome.org.uk

- **Ovarian Cancer Action** - A charity dedicated to improving survival rates for women with ovarian cancer by raising awareness of the disease, giving a voice to women affected by ovarian cancer, and funding research at the Ovarian Cancer Action Research Centre.
  Tel: 0300 456 4700
  Or visit their website at: http://www.ovarian.org.uk/
- **Target Ovarian Cancer** offer information and support for women diagnosed with ovarian cancer. They are establishing regional networks which will raise awareness, campaign for local improvements and fundraise to help more women.
  Their contact details are:
  Tel: 020 7923 5470
  Or visit their website at http://www.targetovarian.org.uk

Table of Study Activities

Activity	Pre-Therapy (Screening) 1st Visit	Cycle*1 Day1 2nd Visit	Cycle*1 Day8 3rd Visit	Cycle*1 Day15 4th Visit	Cycle*1 Day22 5th Visit	Cycle* 2 Day1 6th Visit	Cycle*2 Day15 7th Visit	Cycle*3 Day1 8th Visit	Cycle*3 Day15 9th Visit	Cycle*4 onwards Day1 10th Visit onwards	End of Treatment Visit	28 Day Post Treatment Follow up Visit
Informed consent	X											
General medical and cancer history	X											
Physical examination and disease assessment	X	X		X		X		X		X	X	
Blood pressure and heart rate	X	X	X	X	X	X	X	X	X	X	X	X
Weight and body surface area	X					X		X		X		
Height	X											
Performance status *(Doctor assesses your ability to perform daily tasks)*	X	X		X		X	X	X	X	X	X	x
Urine sample	X	X[1]				X[1]		X[1]		X[1]		
Pregnancy test *(unless unable to have children)*	X	X				X		X		X		
ECG (electrocardiogram) – a painless tracing to assess your heart function	X[3]											
CT/MRI scan	X (then every 8weeks)							X		X	X	
CA125 marker which measures the level of your cancer	X	X				X		X		X	X	
TSH/T4 levels of Thyroid stimulating hormone	X							X[1]		Cycle 6, Day 1, then every 3months[1]		
Echo	X[1]							X[1]		Cycle 6, Day 1, then every 3months[1]		

Activity	Pre-Therapy (Screening) 1st Visit	Cycle*1 Day1 2nd Visit	Cycle*1 Day8 3rd Visit	Cycle*1 Day15 4th Visit	Cycle*1 Day22 5th Visit	Cycle* 2 Day1 6th Visit	Cycle*2 Day15 7th Visit	Cycle*3 Day1 8th Visit	Cycle*3 Day15 9th Visit	Cycle*4 onwards Day1 10th Visit onwards	End of Treatment Visit	28 Day Post Treatment Follow up Visit
Three questionnaires on how you are feeling	X					X		X		X	X	
Other medication you are taking	X	X	X	X	X	X	X	X	X	X	X	X
Assessment of any side effects	X	X	X	X	X	X	X	X	X	X	X	X
Routine blood samples[2]	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	X 30-45 mL (2-3 tbsp.)	
Research blood samples	X 20mL (2 tbsp.)	X 20 mL (2 tbsp.)				X 20 mL (2 tbsp.)		X 20 mL (2 tbsp.)			X 20 mL (2 tbsp.)	
Coagulation blood sample	X[3] 5 mL (1 tsp.)											
Diagnostic cell/tissue sample collection *(archived tissue sample)*	X											

*One cycle is 28 days

[1] When indicated at screening and on Treatment C only (olaparib and cediranib)

[2] On paclitaxel treatment, routine blood tests will only be performed on days 1, 8 and 15 of each cycle

[3] All patients at screening and later only as clinically indicated