ID: UMCC 2018.132	Trabectedin in Combination With Olaparib in Advanced Unresectable or Metastatic Sarcoma	NCT04076579

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: Phase II Trial of Trabectedin in Combination with Olaparib in Advanced Unresectable or Metastatic Soft Tissue Sarcoma

Company or agency sponsoring the study: The University of Michigan along with support from Janssen and AstraZeneca

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigator:
Rashmi Chugh, M.D. Department of Internal Medicine, Hematology/Oncology, University of Michigan

1.1 Key Study Information

You, or your child, may be eligible to take part in a research study. Parents or legal guardians who are giving permission for a child's participation in the research, note that in the sections that follow the word 'you' refers to 'your child'. This form contains information that will help you decide whether to join the study. All information in this form is important. Take time to carefully review this information. After you finish, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your friends, family, or other doctors about your possible participation in this study. If you or your child decides to take part in the study, you will be asked to sign this form. Before you do, be sure you understand what the study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This is a Phase II study, which means the goal is to test the safety and effectiveness of the investigational study drug, in other words - does it work against your type of cancer, and do the benefits outweigh the risks and side effects. This is usually done by comparing the outcomes of subjects in the study to those of people who previously received standard treatment.

This research is studying a new drug combination in small numbers of people to learn about its safety and its effect on your body at certain doses as a treatment for advanced unresectable or metastatic soft tissue sarcoma. This study will be using the drugs olaparib and trabectedin. You will take olaparib orally twice a day, and on certain days you will also be given trabectedin through a pump/port (central venous line) continuously over 24 hours. Others procedures that will take place throughout the course of the study include physical exams, blood

draws, scans of your cancer, urine collection, tests to measure your hearts health along with other items listed later in this document. Your protected health information and tumor tissue will be collected for research purposes.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include diarrhea, vomiting, decreased appetite, fatigue, bruising, pain, headache, rash and abnormal labs test. More detailed information will be provided later in this document.

This study may offer some benefit to you now or others in the future by helping people live longer or improve the quality of life. You may have a beneficial response which may result in longer survival and/or improved quality of life. More information will be provided later in this document. .

We expect the amount of time you will participate in the study to vary depending on how your disease responds to the study intervention and if you have any major side effects up to a maximum of 18 months.

You can decide not to be in this study. Alternatives to joining this study include receiving standard of care treatment, participating in other research trials, if one is available or you may also choose not to receive any further treatment.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

You are being asked to participate in this study because you have been diagnosed with advanced soft tissue sarcoma and treatment with prior chemotherapy has not controlled your tumor. The purpose of this study is to see if the study drugs, trabectedin and olaparib, will shrink your cancer or stop your cancer from growing.

Trabectedin

Trabectedin is also known as Yondelis® and is available by prescription for the treatment of liposarcoma and leiomyosarcoma. We are studying trabectedin/Yondelis ® in combination with olaparib in all types of soft tissue sarcoma. Trabectedin/Yondelis ® works by impairing the function of DNA repair proteins, resulting in cancer cell death.

Olaparib

Olaparib is also known as Lynparza® and is available by prescription for the treatment of breast cancer and ovarian cancer. Olaparib/Lynparza® is being studied in multiple cancers. Olaparib/Lynparza ® works by blocking proteins called PARP. PARP is important for repairing damage to DNA. When this damage is unable to be repaired, the cell dies.

Olaparib is an investigational drug in this study because it has not been approved by the Food and Drug Administration (FDA) for the treatment of sarcomas. The combination of olaparib and trabectedin is investigational in this study because it has not been approved by the FDA for the treatment of sarcomas. This study will test whether combination of these drugs will be effective in shrinking or preventing your tumor from growing.

This is a phase II study, which means the goal is to test the safety and effectiveness of the drug combination.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You are being asked to take part in this study because you are at least 16 years of age and have been diagnosed with advanced soft tissue sarcoma that has not been controlled on prior chemotherapy.

There are many other inclusion and exclusion criteria which the doctors will use to determine if you can participate in this study. It is important that you discuss your full medical history and all of your medications with your doctor.

3.2 How many people (subjects) are expected to take part in this study?

A total of approximately 46 subjects at several institutions will take part in this study, including approximately 30 from the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?
The study team will explain the research study and answer any questions you have about the study. If you want to participate in the study, the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins.

Many of the procedures that will be performed during the study, including routine blood tests, disease evaluations, physical examinations, vital signs and measurement of height and weight, would normally be done as part of your standard of care regardless of study participation. However, some of these may be done more frequently as a result of your participation in this study. Tests and procedures that are done more often than your regular medical care because of your study participation and that are solely for research purposes will be identified below. The study staff will inform you of the types of tests and procedures you have to undergo during the study.

During the study you must:
- Follow the instructions you are given.
- Come to the study center for your visits with the study doctor.
- Tell the study doctor or study staff about any changes in your health and/or medications you are taking.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

Before starting the study: Some exams, tests, and procedures will be required to find out if you can be in this study. If you have had some of the tests recently, they may not need to be repeated. The screening tests and procedures do not have to be completed in one day and you are allowed to take breaks if you have multiple procedures in one day.

The following tests and procedures will be performed during screening and/or at one or more study visits. Refer to the study calendar below for information about which procedures will be performed at certain study visits.

- **Medical history**: including any past treatments, surgeries, infection and autoimmune diseases.
- **Medications**: It is important that you tell your doctor about all of the medications that you have been taking, including over the counter medicines, vitamins or herbal treatments.
- **Physical exam/Vital Signs**: including measurement of your height, weight, blood pressure, heart rate, respiratory rate and temperature.
- **Performance status**: Your ability to perform day to day activities and care for yourself
- **Routine blood tests (approximately 2 teaspoons)**: will be drawn for tests to check blood counts, chemistry, liver and kidney function and creatine phosphokinase
    - If your blood count test results are abnormal for 4 weeks or more after receiving study intervention, your study doctor may refer you to you a hematologist (a doctor who specializes in diseases of the blood). You may also have a **bone marrow biopsy and aspirate** (test involving a thin, hollow needle to withdraw a small amount of bone marrow) for further

testing. If it is not possible for you to have a bone marrow biopsy and aspirate, a **blood sample** will be drawn for testing instead.

- **Blood tests** to see if we can find out more about the health of your heart
- **Urinalysis:** A urine sample for standard laboratory tests to check your general health.
- **Pregnancy test**: (urine or blood – approximately 1 teaspoon): if you are a woman able to have children
- **Scans of your cancer**: these could include Computed tomography (CT) or magnetic resonance imaging (MRI) of the areas of the body involved with your cancer.
    - A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the Radiology Department and takes about half an hour.
    - A MRI scan takes an image of your head or body to observe the location and size of your tumor. For the MRI scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie down on a narrow bed which will slide into a tunnel that is 6 feet long by 22 inches across and is open at each end. You will be asked to lie quietly for about one hour, during which time you will hear a loud machine-like noise. A MRI scan takes about an hour and a half to complete.
- **Echocardiogram**: This procedure captures pictures to assess the heart's function and structures. During an echocardiogram, a wand (like a microphone) sends out sound waves at a frequency too high to be heard. The sound waves bounce or "echo" off of the heart structures and are sent to a computer screen.
- **Electrocardiogram (ECG):** An ECG is a recording of the electrical activity of your heart.
- **Toxicity evaluation:** You will be asked about any side effects or illnesses you experience.
- **Tumor tissue:** Your doctor will check to see if you have enough stored tissue sample of your tumor that was collected previously. You may still participate in this clinical trial even if you do not have enough stored tissue. *This is for research purposes.*

Study Intervention (for Research):
All study subjects will receive both drugs (trabectedin and olaparib).

Trabectedin:
Trabectedin will be administered through a pump/port (central venous line) by a continuous infusion over 24 hours once every 3 weeks (21 days). You will have a port placed prior to initiation of therapy to allow safe delivery of trabectedin. Your dose of trabectedin is calculated based on your height and weight.

Dexamethasone will be given as a pre-medication by infusion approximately 30 min prior to every infusion of trabectedin. Dexamethasone is a cortisone-like drug (a steroid hormone) that may protect you from liver damage related to trabectedin, and may help prevent nausea and vomiting.
Your study team may give you palonosetron or another medication to help lessen or prevent nausea and vomiting. The most common side effects of palonosetron are headache, constipation, diarrhea, dizziness and tired feeling. Ask your study doctor about the side effects of any medication you receive to help prevent nausea and vomiting.

Olaparib:
Olaparib will be dosed by mouth twice daily – once in the morning and once in the evening (approximately 12 hours apart) with or without food.

You will be required to keep a drug diary to track when you take the olaparib. Bring your drug diary and medication bottles (empty and/or with extra tablets), with you when you return for each appointment.

Below are general rules for taking olaparib:

- Take olaparib by mouth twice a day as close as possible to 12 hours apart; preferably at the same time every day
- Take with food (i.e. light meal or snack) or without food
- Avoid grapefruit, its juice and Seville oranges (including marmalade, juice, etc.)
- Swallow whole (do NOT break, chew, crush, dissolve or divide the tablet)
- The medication SHOULD NOT be ingested if broken, cracked or otherwise not intact.
- If you miss a dose (i.e. you do not take it within 2 hours of the scheduled time) DO NOT "make it up". Skip the missed dose and start taking the study drug(s) with the next scheduled dose.
- If you vomit after you take the tablet(s), and you can see that the study drug tablet appears to be complete you can attempt to take the dose for up to 2 hours after the scheduled time. If you cannot take it within 2 hours of the scheduled time DO NOT "make it up". Skip the missed dose and start taking the study drug(s) with the next scheduled dose.

You will continue to take olaparib and trabectedin as long as you do not have any major side effects and your disease has not progressed for up to 18 months.

Follow-up:

If you stop the study intervention for any reason you will be asked to return for end of treatment visit 30 days after your last dose of study intervention.

After you complete the end of treatment visit you will have an office visit or be contacted by a member of the study team every 3 months for up to 2 years from when you stopped the study intervention.
See the table for a summary of the study intervention and procedures.

Study Procedures Table:

Procedures	Screening	Cycle 1 and Cycle 2			Cycle 3+		End of treatment Visit	Follow-Up
		Day 1	Day 8	Day 15	Day 1	Day 15		
Medical History	X	X			X		X	X
Medication Review	X	X			X			
Physical Exam/Vital Signs	X	X			X		X	X
Performance Status	X	X			X		X	X
Electrocardiogram	X							
Routine Blood tests	X	X	X	X	X	X	X	
Blood test to find out about your heart		X			Cycle 3 Day 1 only			
Urinalysis	X							
Pregnancy Test	X	X			X		X	
Scans/Imaging of your Cancer	X	After Cycle 2 (6 weeks) then every 3 cycles (9 weeks)					X	
Echocardiogram	X							
Tumor Tissue	X							
Olaparib		X ----------Taken twice daily in 21 day cycles -------X						
Trabectedin		X			X			
Toxicity Evaluations		X	X	X	X	X	X	
Bone marrow or blood sample		If your blood count test results are abnormal for 4 weeks or more after receiving trabectedin, you may have a bone marrow biopsy and aspirate or a blood sample for further testing.						

OPTIONAL LEFTOVER Research Samples Stored for Unspecified Future Research:
Besides the information about the main study, the following information is specific to unspecified future use of identifiable data and/or biospecimens. We would also like your permission to keep some of your LEFTOVER tumor tissue and medical information collected in the main study, so that we may study it in future research. The future research may be similar to this study or may be completely different.

You can take part in the main study even if you decide not to let us keep your tumor tissue and medical information for future research.

If you give us permission, we will use your tumor tissue and medical information for future research. Even if you give us permission now to keep some of your tissue and medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your tissue, we may not be able to take the information out of our research.

We may share your tumor tissue and medical information with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your blood, tissue and medical information with other researchers, we will not be able to get it back. Future use of your identifiable data and/or specimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your tumor tissue samples. Allowing us to do future research on your tissue and medical information will not benefit you.

With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the future research on your tumor tissue and medical information. You will not have rights to these discoveries or any proceeds from them.

You can make your choice about whether to participate in the Optional substudy (storage of research samples for future use) in Section 12 of the consent.

4.2 How much of my time will be needed to take part in this study?
The initial screening visit will take approximately 4-6 hours. Each study visit is expected to take approximately 2-4 hours. You will be asked to come back every 12 weeks for radiologic disease assessment. If your disease progresses, a member of the study team will either review your medical record or contact you by phone or you will have a clinic visit every 12 weeks for at least 2 years after you started participating in this study.

4.3 When will my participation in the study be over?
You will continue to take olaparib and trabectedin as long as you do not have any major side effects and your disease has not progressed for up to a maximum of 18 months. If you stop the study intervention due to bad side effects or cancer growth, your study doctor will watch you for side effects and follow you closely for at least 30 days or until the side effect has resolved.

We would like to keep track of your medical condition after you stop receiving treatment. A member of the study team may call you on the phone or check your medical record every 3 months for up to 2 years from the time you started participating in this study to see how you are doing. This will allow us to learn about the long-term effects of the drugs. Your participation may end sooner if you decide to no longer participate, your study doctor feels it is in your best interest to stop your study participation, your disease progresses, or the study is ended. You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular physician first.

4.4 What will happen with my information and/or biospecimens used in this study?
Your collected information and biospecimens may be shared with Janssen and AstraZeneca.

Your collected information and biospecimens may also be shared with other researchers, both here or around the world, or with companies. Any sharing is subject to contractual obligations with the Sponsor. Additionally:

- With appropriate permissions, your identifiable collected information and biospecimens may be shared, and/or,
- Without your additional consent, your identifiable private information and identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?
The drugs used in the study may cause certain side effects and discomforts. You may have all, some, or none of the known side effects. There is also a risk that other rare or unknown side effects may occur. Your doctors and nurses will check you closely for side effects and may give you medicines or other treatments to stop or reduce some of these effects. Some side effects may go away soon after the study medication is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent. There is even a chance that a side effect may cause death. If you have any side effects, it is important that you report them to your study doctor or research staff.

These risks will be minimized by monitoring you carefully. We will provide the usual supportive care that would be routinely given to someone with your condition. If you have side effects from the study intervention, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the study intervention if the side effects are too serious.

The known or expected risks are:

Side Effects ASSOCIATED WITH TRABECTEDIN

Over 9,000 patients have been treated with trabectedin either alone or in combination with chemotherapy drugs for the treatment of cancer.

Trabectedin, like many treatments for cancer, can damage normal cells as well as cancer cells. The likelihood of developing side effects will vary from person to person. Most of the trabectedin risks are listed here, but there may be other side effects that we cannot predict.

Common Side Effects (> 20% of study subjects)

- Lowering of blood counts including:
    - Decreased levels of white blood cells (A low white blood cell count may increase the risk that you develop fever, or infection. If the infection is serious, antibiotics or medications to increase the white blood cell count may be necessary).
    - Decreased platelet counts (A low platelet count may make it more likely that you have bleeding and require platelet transfusions).
    - Decreased levels of red blood cells (Low red blood cell counts (anemia) which may cause tiredness and may require blood transfusions).
- Abnormal liver tests
    - Your blood chemistry and liver panels will be monitored frequently during the course of this study in order to identify any liver abnormalities that may develop from the study medication and if any are identified your dose of trabectedin may be reduced or it may need to be discontinued.
- Abnormally increased levels of CPK (an enzyme called creatine phosphokinase) in the blood, a test that may indicate muscle damage.
- Increase in blood creatinine. This test is used to check how your kidneys are working.
- Nausea
- Vomiting
- Tiredness
- Constipation
- Abdominal (belly) pain
- Diarrhea
- Shortness of breath

Occasional Side Effects (> 5% of study subjects)

- Loss of appetite
- Back or joint pain
- Headache
- Fever
- Swelling
- Cough
- Weight loss
- Low levels of potassium in the blood (hypokalemia)
- Dehydration
- Muscle pain (myalgia)
- Dizziness
- Changes in taste of foods (dysgeusia)

- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet (neuropathy peripheral)
- Difficulty falling and/or staying asleep (insomnia)
- Rash
- Hair loss (alopecia)

In a clinical study of trabectedin in patients with soft tissue sarcoma who had previously received a type of chemotherapy treatment known as anthracyclines approximately one of every twenty patients who received trabectedin developed some manifestation of heart dysfunction. It is not clear whether some or all of these occurrences were due to the prior treatment with anthracyclines, which are known to potentially cause heart dysfunction, and whether trabectedin contributed to these events. An uncommon but serious complication of trabectedin could be rhabdomyolysis, which is the breakdown of muscle cells with leakage of potentially toxic contents into the circulation. There have been some deaths reported with this event. There have also been rare cases of death related to trabectedin including multi-organ failure, kidney failure, liver failure, bleeding of the stomach or bowel often in association with low platelets, fluid in the lungs, blood clots in the lungs, and infections in association with low blood counts leading to septic shock and death. Another potentially serious but rare side effect of treatment with trabectedin that may result in death is capillary leak syndrome, a condition that causes fluid to leak out of blood vessels into different tissues which can cause swelling, a sudden drop in blood pressure and a drop in a blood protein called albumin. Other serious and sometimes life-threatening complications that may result in death–although very rarely reported—are severe allergic infusion reactions, or types of blood cancer such as leukemia and myelodysplastic syndrome (MDS).

Trabectedin should be given to you through a central line catheter. If you notice the needle in your venous catheter falls out while trabectedin is being given to you, or that the infusion is leaking from the catheter, tell your doctor immediately. Leakage of trabectedin outside the vein could lead to damage and death of tissue around the injection site (tissue necrosis) that may require surgery. If trabectedin leaks out of your vein, there is no specific treatment to prevent the tissue damage that may occur.

Prior to initiating your treatment in the study, your study doctor will order tests to determine if your cardiac function has been affected from any previous anti-cancer therapies you may have taken, or any medical conditions you may have. If you are at increased risk of cardiac disease, you will be periodically monitored for this toxicity.

Side Effects ASSOCIATED WITH OLAPARIB

Very Common Side Effects (affects more than 1 in 10 patients)

- Diarrhea. If it gets severe, please inform your doctor.
- Nausea/vomiting
- Tiredness/weakness
- Indigestion/heartburn (dyspepsia)
- Headache
- Changes in taste of foods (dysgeusia)
- Dizziness
- Loss of appetite
- Cough
- Pain in the stomach area under the ribs (upper abdominal pain)
- Shortness of breath (dyspnea)
- Constipation

- Abdominal distention or swelling
- Swelling in lower legs or hands
- Urinary tract infection
- Back pain or joint pain (arthralgia)
- Upper respiratory tract infection or (nasopharyngitis)
- Difficulty falling and/or staying asleep (insomnia)
- Pain in Extremity

The following side effects are very commonly shown in blood tests:

- Decrease in the number of red blood cells (anemia) which can be associated with symptoms of shortness of breath, fatigue, pale skin, or fast heartbeat.
- Decrease in the total number of white blood cells (leukopenia) and in certain white blood cells (neutropenia) that protect from infection, which can be associated with symptoms of fever
- Decrease in the number of platelets in blood (thrombocytopenia), which can be associated with symptoms of bruising or bleeding for longer if injured

Common Side Effects (affects up to 1 in 10 patients)

- Sore mouth (stomatitis)
- Rash

The following side effects are commonly shown in blood tests:

- Decrease in the number of white blood cells that support the immune system (lymphopenia), which can be associated with increased susceptibility to infection
- Increase in blood creatinine. This test is used to check how your kidneys are working.

Uncommon Side Effects (affects up to 1 in 100 patients)

- Allergic reactions
- Itchy rash on swollen, reddened skin (dermatitis)

The following side effects are uncommonly shown in blood tests:

- Increase in the size of red blood cells (not associated with any symptoms)

The Study Doctor may decide to interrupt and/or reduce your olaparib dose if you experience certain side effects. If your dose is reduced, you will be given a new bottle of tablets.

Driving and using machines

The study drug may affect your ability to drive or use machines. If you feel dizzy, weak, or tired while taking your study treatment, take special care when driving or using tools or machines.

Other potential risks

Other side effects have been seen in previous studies, but it is not yet known if these were related to olaparib, or if they were unrelated events possibly due to the patient's cancer or other cause. Assessing the full range of side effects of olaparib is an important part of this study.

Pneumonitis (lung inflammation) has been reported in a small number of patients treated with olaparib in previous studies, and some reports have been fatal. It is not known if olaparib caused the pneumonitis in these

patients as they had other possible causes such as lung cancer and/or metastases in the lungs, pre-existing lung disease, were smokers, or had been treated previously with chemotherapy or radiotherapy. If you experience any new or worsening symptoms of shortness of breath, cough and fever, you should contact your Study Doctor as soon as you can.

Myelodysplastic syndrome and acute myeloid leukaemia: These side effects have been reported in a small number of patients treated with olaparib in previous studies and the majority of cases have been fatal. It is not known if olaparib caused myelodysplastic syndrome and/or acute myeloid leukaemia in these patients as they had other possible causes, in particular they had received extensive previous chemotherapy. 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.

- 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). This condition has the potential to transform into acute myeloid leukaemia
- 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.

Side Effects ASSOCIATED WITH DEXAMETHASONE

Most Common Side Effects

- Muscle weakness
- Headache
- Water retention
- Stomach irritation
- Increased blood sugar levels.

Risks of CT Scan

The contrast substance injected during the CT scan may cause pain, burning feeling, sweating and rarely a serious allergic reaction that can be serious. If you know you're allergic to iodine you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you're diabetic, dehydrated and if you're older. In addition, your thyroid function may be affected. Please inform your doctor if this is the case.

CT imaging uses ionizing radiation, which increases your risk to develop cancer. Everyone is exposed to naturally occurring ionizing radiation every day. The amount of radiation exposure from 1 CT scan is approximately comparable to 1-3 years of natural background radiation. The estimated additional lifetime risk of developing a fatal cancer from a standard CT scan is approximately 1 in 2,000.

Risks of MRI Scan

Contrast is used to improve the pictures of the inside of the body made by the MRI. Common risks of MRI include: feeling fearful of being in a small enclosed space (claustrophobia) when you are lying inside the MRI scanner, feeling uncomfortable because of the loud noises made by the machines, and feeling uncomfortable with the physical sensations you may feel during the process. You are also exposed to some risk because of the injected contrast, gadolinium-DTPA, which may cause headache, nausea, and local burning sensation.

The contrast agent, gadolinium has been linked to development of Nephrogenic Fibrosing Dermopathy (NFD) (also known as Nephrogenic Systemic Fibrosis (NSF) This causes a thickening of the skin, organs and other tissues, and is a rare complication in patients with kidney disease that undergo an MRI with contrast material. To help prevent this, we will check how well your kidneys work before you have any MRIs. Because of the use of contrast, all female subjects who are able to have children will be required to use adequate birth control. If you have implanted metal objects such as a pacemaker, artificial limbs, or metal joints, you will not be able to have an MRI done, and may not be able to take part in this research.

Blood tests
Collection of blood samples may cause pain, bleeding, bruising or infection. It is also possible that you may feel lightheaded or faint. Please tell your study doctor or the study nurse if you do not feel well after having blood drawn at any time during your study participation.

Echocardiogram (ECHO)
An ECHO is a test that uses sound waves to create a moving picture of the heart, also called a cardiac ultrasound. This test is done to assess how well your heart functions. You may feel some discomfort due to the specific position you may hold during the exam.

Electrocardiogram (ECG)
An ECG shows the electrical activity of the heart by placing several small adhesive pads that are attached to wires on your chest and limbs (called leads) and connecting them to a machine that reads the signal. There may be minor discomfort, similar to removing a bandage, when the electrodes taped to your chest are removed.

Bone Marrow Aspirate/Biopsy:
Will only be done if your blood count test results are abnormal for 4 weeks or more after receiving study intervention.

You may feel some amount of pain or discomfort during the aspiration or biopsy, including slight, stinging pain with the local anesthetic is injected by needle to numb the area, pressure and full pain where the biopsy needle is inserted, discomfort from lying still for an extended time, and soreness at the biopsy site. If a conscious sedation medication is used, you will not feel pain during the procedure because you will be asleep. Your study doctor will explain the details of the procedure and the risks to you, depending on how the bone marrow aspirate and biopsy will be obtained.

Other risks include redness, swelling, excessive bleeding, bruising or draining at the needle site, abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site.

Research samples/Loss of Confidentiality
Your samples will be coded, however, there is a risk of loss of confidentiality of your information. If your samples are provided to research collaborators the following information may be made available: your diagnosis and treatments, the time the samples were collected in relation to your study regimen, your disease status, and demographic data (for example gender, race, age, etc.). See section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

Pregnancy
WOMEN

The risk of trabectedin and olaparib to the fetus has not been determined. However, based on its known mechanism of action, trabectedin and olaparib have the potential to cause serious birth defects when given during pregnancy. If you are a woman, you will not be allowed to participate in this study if you are pregnant or breastfeeding as taking part in this study might harm your unborn child or breast-fed baby. You must agree not to become pregnant while you are in this study.

If you become pregnant or think you may be pregnant during the study, immediately stop using the study drugs and contact the study doctor's office **immediately**. You must not breast-feed an infant during the study. Please also inform the study doctor if you become pregnant up to 5 months after the completion of the study drugs. If there is ANY chance that you can get pregnant, you must either agree to not have vaginal intercourse or you must use TWO types of birth control (one from each list below) AT THE SAME TIME throughout the study and for 6 months after the last dose of study drugs.

Primary forms
- tubal sterilization (tubes tied)
- partner's vasectomy
- intrauterine device

Secondary forms
- male latex condom with or without spermicide
- diaphragm with spermicide
- cervical cap with spermicide
- vaginal sponge (contains spermicide)

Any birth control method can fail. The reports of birth control failing are more frequent for female patients who use only a single form of birth control. Using two forms of birth control at the same time greatly reduces the chances of pregnancy.

MEN
All men and their partners must use TWO types of birth control (one from each list above) AT THE SAME TIME while taking part in the study and for 5 months after treatment has stopped because the effects on sperm are not known. Acceptable forms of birth control are male latex condom (with or without spermicide) or vasectomy. Also, men should not donate sperm or semen while taking part in the study and for 5 months after treatment has stopped because the effects on sperm are not known.

ALL SUBJECTS
The study doctor must follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished. If you become pregnant during the study or up to 5 months after you stopped taking the study drugs, the study doctor or his/her staff will ask to contact you and your pregnancy physician for information about the pregnancy until the child is born and may share this information with the sponsor.

If you are male, you should advise your study doctor if you father a child while participating in this study and for up to 5 months after study treatment has stopped. The doctor will advise you on medical attention for your partner should this be necessary. We will ask for your partner's permission to collect information about the pregnancy and health of the baby.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
This study may offer some benefit to you now or others in the future. You may have a beneficial response which may result in longer survival and/or improved quality of life.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?
You do not have to be in this study to get treatment for your cancer. Other possible options include:

- There may be other treatment options which depend on the kind of soft tissue sarcoma you have: single-agent trabectedin, dacarbazine, pazopanib, or doxorubicin. You should discuss this with your doctor.
- There may be other clinical trials available for you. You should also discuss this with your doctor.
- If no further disease-specific treatment option is available, getting comfort care, also called palliative care, is an option. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible

You should talk to your study doctor and your regular physician about each of your options and their risks and benefits before you decide if you want to take part in this study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information” (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
If you decide to leave the study early, please notify someone on the study team. They will instruct you on how to stop the study safely and you will be advised whether any additional test may need to be done for your safety.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

Olaparib will be provided by AstraZeneca free of charge.

Trabectedin will be provided by Janssen free of charge
You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices (such as the cost of the infusion)
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services
- Treatment of complications

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
You will not be paid to take part in this study.

8.3 Who could profit or financially benefit from the study results?

Information obtained from this study may help the supporters Janssen and AstraZeneca and/or the University of Michigan learn more about the causes, risks, treatments, or how to prevent this and other health problems. In the interest of transparency, we'd like you to know that Dr. Chugh was paid to consult for Janssen at a one-time meeting.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

The University of Michigan has rules to protect information about you. Federal and state laws also protect your privacy. Upon enrolling in this study, you will be assigned a unique identification number. All records related to the study will use this identification number instead of your name or other personally identifying information whenever possible. We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file.

You have the right to request access to your protected health information that is used or shared during this research and that is related to your study treatment for your disease, but you may access this information only after the study is completed. To request this information, please contact the researchers listed in Section 10 “Contact Information” (below).

Genetic Risks:

The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups; however, these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

We *may* collect and store information about your genes. The DNA contained in your genes holds the instructions that your body uses to grow and function. Your genes are responsible for your physical features such as eye color, blood type, and how your body breaks down medications. Genes can also be responsible for some medical conditions.

Genomic information relates to the structure and function of all of the genetic material in the body.

We may submit your genomic information to a repository to be used for scientific purposes. A repository contains information from many people. Some repositories are maintained by the University of Michigan, some are maintained by the federal government, and some are maintained by private companies.

Researchers all over the world can take information from the repository and use it in their studies. Their studies may be similar to this one or may be completely different.

Some data collected from you may be deposited into the database of Genotypes and Phenotypes (dbGAP) but all identifiable information will be removed prior to submission so that the data cannot be linked to you in any way. The database of dbGaP is a database developed by the National Center for Biotechnology Information (a division of the National Library of Medicine) to archive and distribute the results of studies that have investigated the interaction of genotype and phenotype. All data submitted from this study will only be available through controlled access and restricted to cancer research studies. Any researcher requesting access to the data must formally apply to dbGAP and present a research study rationale for why they need access to the data. The data may also be submitted to other future database systems which will have similar access controls as dbGAP utilizes. Genomic summary results should be kept restrictive.

We will label your genomic information with a code, instead of your name or other information that people could use to directly identify you. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally.

If you allow us to put your genomic information in the repository, you can change your mind later and ask us to remove it. Keep in mind, however, that we cannot take back information that other researchers have already obtained from the repository.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- HIV/AIDS status
- Sexually transmitted disease or other communicable disease status
- Health plan/health insurance records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University of Michigan, Food and Drug Administration (FDA), and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Janssen, AstraZeneca, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular University of Michigan medical record.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission, or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information

- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help the University of Michigan and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa.

9.4 When does my permission expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:	Rashmi Chugh, MD
Mailing Address:	University of Michigan C407 MIB 1500 E. Medical Center Drive Ann Arbor, MI 48109-0848
Telephone:	734-936-0453
Hospital Operator:	734-936-4000 (24-hour paging)

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received signed and dated copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*
- Other (specify):_____

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with:_____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____
(16-17 Assenting)

Date of Signature (mm/dd/yy): _____

Consent/Assent to Collect and Store OPTIONAL Research Samples for Unspecified Future Research
This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to take part in this optional research. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep and store my tissue samples for future research.

_____ No, I do not agree to let the study team keep and store my tissue samples for future research.

Print Legal Name: _____

Signature: _____
(16-17 Assenting)

Date of Signature (mm/dd/yy): _____

Legally Authorized Representative or Parent Permission

Subject Name: _____

Parent/Legally Authorized Representative:

Name: _____

Signature: _____

Address: _____

Date of Signature (mm/dd/yy): _____

Relationship to subject: Parent Spouse Child Sibling Legal guardian Other

If "Other," explain: _____

Reason subject is unable to consent: _____

If this consent is for a child who is a ward of the state (for example, a foster child), please tell the study team immediately. The researchers may need to contact IRBMED.

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____