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June 28, 2024

Dr. Elise C. Kohn, MD
Cancer Therapy Evaluation Program
9609 Medical Center Drive
NCI Shady Grove Room 5W426
Rockville, MD 20850

Re: Review of Amendment #06 of Protocol #A092104: "A Randomized Phase 2/3 Study of Olaparib Plus Temozolomide Versus Investigator's Choice for the Treatment of Patients with Advanced Uterine Leiomyosarcoma After Progression on Prior Chemotherapy"

Dear Dr. Kohn,

We would like to thank the CTEP Reviewers for the December 21, 2023 review of the protocol and consent associated with the Alliance A092104 trial, "*A Randomized Phase 2/3 Study of Olaparib Plus Temozolomide Versus Investigator's Choice for the Treatment of Patients with Advanced Uterine Leiomyosarcoma After Progression on Prior Chemotherapy*." The Study Team's responses to each comment are included in bold text with references to each section of the protocol or consent that will contain the revision.

Please let us know what further information we may provide.

Sincerely,

Stephanie Berg, MD
Executive Officer
Alliance for Clinical Trials in Oncology

I. Recommendations:

#	Section	Comments
1.	6.1.2 Medidata Rave	***Please revise the following language:*** Medidata Rave is the clinical data management system being used for data collection for this trial/study. Access to the trial in Rave is controlled through the CTEP-IAM system and role assignments. Requirements to access Rave via iMedidata: Active CTEP registration with the credentials necessary to access secure NCI/CTSU IT systems and Assigned a Rave role on the LPO or PO roster at the enrolling site of: Rave CRA, Rave Read Only, Rave CRA (LabAdmin), Rave SLA, or Rave Investigator. Rave role requirements: Rave CRA or Rave CRA (Lab Admin) role must have a minimum of an Associate Plus (AP) registration type; Rave Investigator role must be registered as an Non-Physician Investigator (NPIVR) or Investigator (IVR); and Rave Read Only or RAVE SLA role must have at a minimum an Associates (A) registration type. Refer to https://ctep.cancer.gov/investigatorResources/default.htm for registration types and documentation required. This study has a Delegation of Tasks Log (DTL). Therefore, those requiring write access to Rave must also be assigned the appropriate Rave tasks on the DTL. ~~Upon initial site registration approval for the study in the Regulatory application, all persons with Rave roles assigned on the appropriate roster will be sent a study invitation email from iMedidata. To accept the invitation, site staff must either click on the link in the email or log in to iMedidata via the CTSU members' website under *Data Management > Rave Home* and click to *accept* the invitation in the *Tasks* pane located in the upper right corner of the iMedidata screen.~~ Upon initial site registration approval for the study in the Regulatory application, all persons with Rave roles assigned on the appropriate roster will be sent a study invitation email from iMedidata. No action will be required; each study invitation will be automatically accepted and study access in Rave will be automatically granted. Site staff will not be able to access the study in Rave until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learnings (eLearnings) and can be accessed by clicking on the eLearning link in the *Tasks* pane located in the upper right corner of the iMedidata screen. If an eLearning is required for a

#	Section	Comments
		study and has not yet been taken, the link to the eLearning will appear under the study name in the *Studies* pane located in the center of the iMedidata screen; once the successful completion of the eLearning has been recorded, access to the study in Rave will be granted, and a *Rave EDC* link will replace the eLearning link under the study name. ~~Site staff who have not previously activated their iMedidata/Rave account at the time of initial site registration approval for the study in the Regulatory application will receive a separate invitation from iMedidata to activate their account. Account activation instructions are located on the CTSU website in the Data Management section under the Rave resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on iMedidata/Rave is available on the CTSU members' website in the Data Management > Rave section or by contacting the CTSU Help Desk at 1-888-823-5923 or by email at ctsucontact@westat.com.~~ No action will be required by site staff (to activate their account) who have not previously activated their iMedidata/Rave account at the time of initial site registration approval for the study in the Regulatory application. Pending study invitations (previously sent but not accepted or declined by a site user) will be automatically accepted and study access in Rave will be automatically granted for the site user. Account activation instructions are located on the CTSU website in the *Data Management* section under the Data Management Help Topics > Rave resource materials (*Medidata Account Activation and Study Invitation*). Additional information on iMedidata/Rave is available on the CTSU members' website in the *Data Management > Rave section* or by contacting the CTSU Help Desk at 1-888-823-5923 or by email at ctsucontact@westat.com. **PI Response: The above language has been incorporated into Section 6.1.2 based upon current CTSU boilerplate language.**
2.	Appendix V	For the pazopanib medication diary, please change "Take consistently with or without food" to "Take consistently without food." The prescribing information clearly states to take without food. In the adherence section at the bottom, change "twice daily" to "once daily" since this agent is not administered BID. **PI Response: The above requested changes have been made to Appendix V.**

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

PROTOCOL UPDATE TO ALLIANCE A092104

A RANDOMIZED PHASE 2/3 STUDY OF OLAPARIB PLUS TEMOZOLOMIDE VERSUS INVESTIGATOR'S CHOICE FOR THE TREATMENT OF PATIENTS WITH ADVANCED UTERINE LEIOMYOSARCOMA AFTER PROGRESSION ON PRIOR CHEMOTHERAPY

[X] **Update:**	[ ] **Status Change:**
[ ] Eligibility changes	[ ] Pre-Activation
[X] Therapy / Dose Modifications / Study Calendar changes	[ ] Activation
[X] Informed Consent changes	[ ] Closure
[ ] Scientific / Statistical Considerations changes	[ ] Suspension / temporary closure
[ ] Data Submission / Forms changes	[ ] Reactivation
[X] Editorial / Administrative changes	
[X] Other: CTSU boilerplate language updates	

No recommended IRB level of review is provided by the Alliance since the CIRB is the IRB of record for this trial.

The site has 30 days after the posting of this amendment to implement it at their site. Please refer to the amendment application and CIRB guidelines for further instructions.

UPDATES TO THE PROTOCOL

Title Page

- The NCT number has been corrected to NCT05432791 ~~NCT05633381~~.
- Kristen N. Ganjoo, MD has been added to the cover page as the ECOG-ACRIN Study Champion and contact information has been updated accordingly.
- The institution site and telephone numbers for the A092104 Committee Chairs, Committee Modalities, have been removed to align with the current Alliance protocol template.

Study Resources

- In the Protocol Contacts box, the institution site and telephone number for the A092104 Nursing Contact and the A092104 Pharmacy Contact have been removed to align with the current Alliance protocol template and in the first box under "Contact via email," the personnel list has been reformatted.

- In the Protocol Contacts box the Alliance Biorepository room number has been updated to, "~~1H-05-35~~5120."

CTSU Address and Contact Information

- The table has been completely updated to reflect updated CTSU boilerplate language.
- The third box has been updated to, "Institutions will obtain the following supplies from the CTSU website: PRO CTCAE can be obtained by downloading the booklet from the protocol-specific page on the CTSU website ~~Supplies can be ordered by downloading and completing the CTSU Supply Request Form (available on the protocol-specific page on the CTSU website) and submitting it as instructed on the form~~."

Section 4.0 (Patient Registration)

The following subsections have been updated to reflect the updated CTSU boilerplate language:

- Section 4.1 (Investigator and Research Associate R~~r~~egistration with CTEP)
- Section 4.2 (Cancer Trials Support Unit R~~r~~egistration P~~p~~rocedures)
- Section 4.2.1 (Additional S~~s~~ite R~~r~~egistration R~~r~~equirements)
- Section 4.2.2 (Downloading Site Registration Documents)
- Section 4.2.3 (Submitting R~~r~~egulatory D~~d~~ocuments)
- Section 4.2.4 (Checking S~~s~~ite's R~~r~~egistration S~~s~~tatus)
- Section 4.2.5 (Delegation of Task Log (DTL))
- Section 4.4 (Patient Enrollment ~~registration/randomization procedures~~)

Section 4.3.2 (Patient-reported outcomes)

In the sub-section "Patient questionnaire booklets," the entire paragraph has been rewritten to remove instructions for ordering the PRO-CTCAE booklets from CTSU and has been revised to instructions about downloading the PRO-CTCAE booklets from CTSU.

Section 5.0

- In Study Calendar Arm 1: Olaparib + Temozolomide, footnote # 3 has been completely updated to reflect the most current Alliance template language for medication diaries.
- In Study Calendar Arm 2: Pazopanib, footnote # 3 has been completely updated to reflect the most current Alliance template language for medication diaries.

Section 6.0 (Data and Specimen Submission)

The following subsections have been updated to reflect the updated CTSU boilerplate language:

- Section 6.1.2 (Medidata Rave)
- Section 6.1.3 (Data Quality Portal)

6.2.1 (Overview of Specimen Requirements)

Footnote 1 has been added to the specimen table clarifying that buffy coat is required only at one time point.

Section 6.3 (Submission of Patient Completed Measures)

The second paragraph has been revised to remove the ordering of booklets through CTSU. The paragraph now reads as follows: Patient-completed questionnaire booklets for this study are to be ~~ordered~~ downloaded prior to the registration of any patients (see Section 4.3.2, Patient-reported outcomes). ~~Samples of questionnaire booklets are available in Appendix VI for reference and IRB submission only. They are not to be used for patient completion.~~ Booklets must be given to patients to complete and patients should be

instructed to return the booklets/responses to site staff (in person, by mail, or by phone) and site staff will enter patient responses into Medidata Rave. The method of administration (in person, by mail, etc.) should be documented in the source documents. At visits in which booklets are to be completed, the booklet should be given to the patient before any discussion of the patient's health status or test results. The method of collection should be documented in Rave.

Section 7.1 (Arm 1 (Olaparib + Temozolomide))

- The second paragraph has been updated to identify the abbreviated acronym for temozolomide, it now reads, "Temozolomide (TMZ) is administered at 75 mg/m^2 orally…"
- In the Regimen Description box, in the second column, the premedication instructions for Temozolomide have been clarified as follows, "Ondansetron 8 mg PO once prior to TMZ (required during cycle #1, optional thereafter). TMZ can be taken with or without food but it may be better tolerated if taken on an empty stomach. Take TMZ with a full glass of water with the AM dose of olaparib; or if nausea is a difficulty, take TMZ with or without food with the PM dose of olaparib. Recommend consistency daily regarding with or without food and regarding AM or PM dosing.
- The first paragraph under the "Temozolomide" sub-heading has been updated for clarity. The clarifications are as follows: "Patients will be administered TMZ once daily (QD). The TMZ capsules should be swallowed whole with a glass of water and not opened, crushed, ~~or~~ chewed, or dissolved. ~~To reduce nausea,~~ TMZ can be taken with or without food, but if there are issues with nausea, fasting is recommended (should be taken on an empty stomach ~~(~~[i.e. in the fasted state, either 1 hour before, or 2 hours after, a meal]). This includes when taking temozolomide with olaparib. Patients should take ondansetron 8 mg PO once concurrently or up to 30 minutes before the TMZ dose during cycle 1. If vomiting occurs, do not repeat dose, patients should wait until next scheduled dose."
- Under the sub-heading "Olaparib" the fifth sentence has been updated to," Olaparib tablets can be taken with or without food; however, since the morning dose is taken with TMZ, both agents ~~will~~ should be taken together on an empty stomach for the morning dose. If taken with or without food, it should consistently be taken in that manner."

Section 7.2 (Arm 2 (Investigator's Choice: Trabectedin or Pazopanib))

Under the sub-section "Pazopanib", a new fourth paragraph for dosing has been added for clarity.

Section 9.0 (Adverse Events)

Section 9.1.1 (Rave CTEP-AERS integration) has been updated to reflect the updated CTSU boilerplate language.

Appendix III (A092104 Olaparib Medication Diary)

- Instruction #2, the second sentence has been updated to, "The morning One dose of olaparib ~~will~~ should be taken together with temozolomide at approximately the same time (morning or night of each day."
- Instruction #3, has been updated to, "Your dose of olaparib is ____ mg twice daily which ~~will~~ should be taken…"
- Instruction #4 has been updated with additional instructions for medication dosing. The instructions that have been added are as follows: "This includes when taking olaparib with **temozolomide**. Temozolomide can be taken with or without food but it may be better tolerated if taken on an empty stomach."

- On the calendar the header in the third and fifth columns have been updated to, "Number of olaparib tablets taken in the Morning/Evening."

Appendix IV (A092104 Temozolomide Medication Diary)

- Instruction #2, the second sentence has been updated to, "Temozolomide ~~will~~ should be taken together with the morning dose **or the evening dose of olaparib, at approximately the same time each day**"
- Instruction #4 has been updated with additional instructions for medication dosing. The updated instructions are as follows: "You will take your dose of **temozolomide once a day for 7 consecutive days followed by 14 days off.** ~~Take consistently with or without food~~ Temozolomide can be taken with or without food, but it may be better tolerated if taken on an empty stomach [(i.e. in the fasted state, either 1 hour before, or 2 hours after, a meal]). Take consistently with or without food. This includes when taking **olaparib** with temozolomide. For the first cycle of treatment, take ondansetron 8 mg approximately 30 minutes prior to taking the temozolomide to help prevent nausea. From cycle 2 onward, the use of ondansetron prior to temozolomide dosing is optional
- On the calendar the header in the third, fourth, and fifth columns have been updated to, "Number of temozolomide capsules taken."

Appendix V (A092104 Pazopanib Medication Diary)

- Instruction #2, has been updated to, "Your dose of pazopanib is ____ mg once daily which ~~will~~ should be taken…"
- On the calendar the header in the third and fifth columns have been updated to, "Number of pazopanib tablets taken in the Morning/Evening.
- In the signature box, under "To be completed by staff, the following has been corrected, Total Daily Dose:_____ mg ~~twice~~ once daily

Appendix VI (PRO-CTCAE)

- Appendix IV has been completely removed as PRO-CTCAE booklets for English and Spanish are available for download or ordering from the CTSU.
- The remaining appendices have been renumbered.

UPDATES TO THE MODEL CONSENT:

Title Page

- The NCT number has been corrected to NCT05432791 ~~NCT05633381~~.

A replacement protocol document and model consent form have been issued.

ATTACH TO THE FRONT OF EVERY COPY OF THIS PROTOCOL

Research Study Informed Consent Document

Study Title for Participants: Testing olaparib and temozolomide versus the usual treatment for uterine leiomyosarcoma after chemotherapy has stopped working

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: A092104: "A randomized phase 2/3 study of olaparib plus temozolomide versus investigator's choice for the treatment of patients with advanced uterine leiomyosarcoma after progression on prior chemotherapy (NCT05432791)"

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have uterine leiomyosarcoma that has grown after initial treatment with two prior forms of chemotherapy and cannot be removed by surgery.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

This study is conducted by the Alliance for Clinical Trials in Oncology, a national clinical research group supported by the National Cancer Institute. The Alliance is made up of cancer doctors, health professionals, and laboratory researchers, whose goal is to develop better treatments for cancer, to prevent cancer, to reduce side effects from cancer, and to improve the quality of life of cancer patients.

Why is this study being done?

This study is being done to answer the following question:

Is the combination of olaparib and temozolomide better than the usual treatment for advanced uterine leiomyosarcoma after initial chemotherapy has stopped working?

We are doing this study because we want to find out if the combination of olaparib and temozolomide is better, worse or the same than the usual approach for advanced uterine leiomyosarcoma. The usual approach is defined as care most people get for uterine leiomyosarcoma.

What is the usual approach to my uterine leiomyosarcoma?

The usual approach for patients who are not in a study is additional treatment with other chemotherapy drugs, most commonly with one of two chemotherapy drugs: trabectedin or pazopanib. Trabectedin and pazopanib are both FDA-approved drugs that have been shown to help patients with advanced uterine leiomyosarcoma. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get the combination of olaparib and temozolomide or the usual treatment for uterine leiomyosarcoma until your cancer gets worse or the side effects become too severe. If you receive the usual treatment, you will receive either trabectedin or pazopanib, and the choice will be made by you and your doctor together.

After you finish your study treatment, your doctor will continue to follow your condition and watch you for side effects for up to 5 years. Your doctor and/or a member of the research team will contact you every 3 months for up to 5 years after you finish your study treatment to ask about this information.

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

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the “What risks can I expect from taking part in this study?” section.

If you choose to take part in this study, there is a risk that olaparib and temozolomide may not be as good as the usual approach at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from olaparib and temozolomide. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects from olaparib and temozolomide that the study doctors know about are:

- Anemia ("low red blood cell count"), which may require blood transfusion
- Diarrhea, constipation, nausea and/or vomiting
- Difficulty sleeping
- Dizziness
- Hair loss
- Loss of appetite
- Muscle weakness
- Tiredness
- Trouble with memory

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that olaparib and temozolomide may be effective in shrinking or stabilizing your type of cancer. However, we do not know if olaparib and temozolomide will extend your life compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.

- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (Alliance for Clinical Trials in Oncology). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare an investigational treatment, olaparib and temozolomide, to the usual treatment for uterine leiomyosarcoma after two types of chemotherapy have stopped working. This study will help study doctors find out if this different approach is better, the same, or worse than the usual approach. To decide if it is better, the study doctors will be looking to see if olaparib and temozolomide lengthens the time it takes for the cancer to get worse, or lengthens overall survival, for patients with this type of cancer.

There will be about 190 people taking part in this study.

What are the study groups?

This study has 2 study groups. You will be told which group you are in.

- **Group 1**

  If you are in this group, you will get the combination of olaparib and temozolomide. Olaparib is a pill taken twice per day. Temozolomide is also a pill and is taken once per day. Both drugs are taken for 7 days in a row followed by 14 days off. Olaparib and temozolomide will be given in 21-day cycles that repeat until the drugs stop working or cause too many side effects.

  You will not be able to get additional doses of olaparib. Olaparib with temozolomide is not approved by the FDA for treatment of your disease. Temozolomide alone is sometimes used as a usual treatment for your disease.

  There will be about 95 people in this group.

- **Group 2**

  If you are in this group, you will get one of the two the usual drugs used to treat this type of cancer: trabectedin or pazopanib.

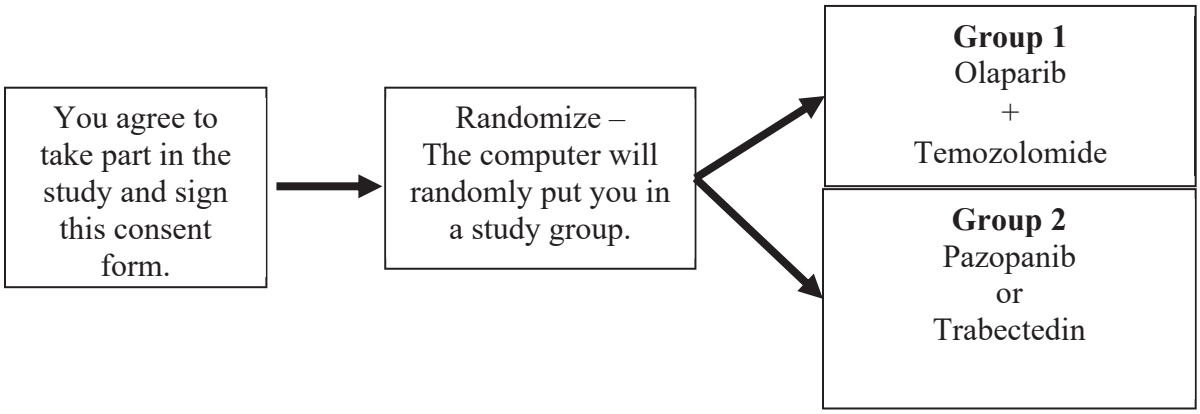
Trabectedin and pazopanib are both FDA-approved drugs that have been shown to help people with uterine leiomyosarcoma. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer. You and your doctor will together decide which drug is the best choice for you.

Trabectedin is administered as a 24 hour continuous ambulatory (outpatient) infusion through a port and is repeated once every 21 days. Pazopanib is a pill that you take by mouth once every day. During this study, both trabectedin and pazopanib will be given in 21-day cycles that repeat until the drug stops working or causes too many side effects.

There will be about 95 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

- **Paper surveys:** For this study, English and Spanish readers will be asked to complete questionnaires about side effects you may be experiencing on a paper survey. The paper survey will be performed once before treatment starts, at the beginning of each

cycle of treatment (until cycle 11), and once after treatment ends. It will take approximately 10 minutes to complete this survey.

Since these forms are being used for research, the responses you provide will not be shared with your study doctor. If you have any serious health issues or other concerns, please talk with your doctor or nurse right away.

You will be asked to fill out this form at 13 times:

- Before treatment begins
- At the beginning of each cycle of treatment (until cycle 11)
- After treatment ends

Each form will take about 10 minutes to complete. The forms will ask about things like (briefly describe, e.g., tiredness, diarrhea). You don't have to answer any question that make you feel uncomfortable.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that olaparib and temozolomide may not be as good as the usual approach at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 3 months after you have completed the study.

Side Effect Risks

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.

2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 - Possible side effects of Olaparib and Temozolomide are listed in the tables below:

Possible Side Effects of Olaparib (AZD2281)
(Table Version Date: June 5, 2023)

COMMON, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Pain • Diarrhea, nausea, vomiting • Tiredness • Loss of appetite

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), from 4 to 20 may have:

• Bloating, constipation, heartburn • Sores in the mouth which may cause difficulty swallowing • Swelling of arms, legs • Cold symptoms such as stuffy nose, sneezing, sore throat • Infection which may cause painful and frequent urination • Infection, especially when white blood cell count is low • Dizziness, headache • Changes in taste • Cough, shortness of breath • Rash

RARE, AND SERIOUS In 100 people receiving olaparib (AZD2281), 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Bruising, bleeding • Cancer of bone marrow caused by chemotherapy • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Damage to the lungs which may cause shortness of breath • Blood clot

Possible Side Effects of Temozolomide
(Table Version Date: September 28, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving temozolomide, more than 20 and up to 100 may have:
• Constipation, nausea, vomiting, diarrhea • Dizziness • Muscle weakness, paralysis, difficulty walking • Trouble with memory • Tiredness • Difficulty sleeping • Hair loss • Headache and seizure

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving temozolomide, from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require transfusion • Bruising, bleeding • Severe skin rash with blisters and can involve inside of mouth and other parts of the body • Rash

RARE, AND SERIOUS In 100 people receiving temozolomide, 3 or fewer may have:
• Cancer of bone marrow caused by the chemotherapy • Damage to the bone marrow (irreversible) which may cause infection, and bleeding, may require blood transfusions • Liver damage which may cause yellowing of eyes and skin, swelling • Cough, damage to the lungs which may cause shortness of breath

Study Group 2 – Possible side effects of Pazopanib and Trabectedin are listed in the tables below. These drugs are the usual approach for treating this type of cancer:

Possible Side Effects of Pazopanib
(Table Version Date: June 8, 2023)

COMMON, SOME MAY BE SERIOUS In 100 people receiving pazopanib (GW786034), more than 20 and up to 100 may have:
• Diarrhea, nausea, vomiting • Tiredness • Bruising, bleeding • Infection, especially when white blood cell count is low • Loss of appetite • Change in hair color • High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pazopanib (GW786034), from 4 to 20 may have:

- Anemia which may require blood transfusion
- Abnormal heartbeat
- Pain
- Constipation, heartburn
- Sores in the mouth which may cause difficulty swallowing
- Swelling of arms, legs
- Fever
- Weight loss
- Dehydration
- Dizziness, headache
- Changes in taste
- Cough, shortness of breath
- Internal bleeding which may cause coughing up blood, black tarry stool, blood in vomit or blood in urine
- Bleeding from multiple sites including nose or vagina which may cause blurred vision with a chance of blindness
- Hair loss, rash, skin changes
- Redness, pain or peeling of palms and soles

RARE, AND SERIOUS
In 100 people receiving pazopanib (GW786034), 3 or fewer may have:

- Anemia, kidney problems which may cause tiredness, bruising, swelling, or may require dialysis
- Blood clot which may cause confusion, paralysis, seizures or swelling, pain, shortness of breath
- Change in the heart rhythm
- Heart failure, heart attack which may cause shortness of breath, swelling of ankles, and tiredness
- A tear or hole in internal organs that may require surgery
- Liver damage which may cause yellowing of eyes and skin, swelling
- Change in heart function
- Kidney damage which may require dialysis
- Bleeding in the brain
- Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Damage to the lungs which may cause shortness of breath
- Blood clot in artery which may cause swelling, pain, shortness of breath or change of color in extremity
- Weakening of artery which may cause bleeding

Possible Side Effects of Trabectedin
(Table Version Date: July 22, 2022)

COMMON, SOME MAY BE SERIOUS
In 100 people receiving trabectedin, more than 20 and up to 100 may have:

• Nausea • Vomiting • Constipation • Diarrhea • Fatigue • Edema of the legs or arms (peripheral edema) • Decreased appetite • Shortness of breath • Headache • Increase in liver enzymes, reflecting damage or irritation to the liver • Low red blood cells (anemia) • Low levels of cells that fight infection (neutropenia) • Low levels of platelets (cells that stop bleeding)

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving trabectedin, from 4 to 20 may have:
• Muscle aches and pains • Difficulty sleeping • Infection with low levels of white blood cells (“febrile neutropenia”) • Muscle breakdown, which may cause pain and kidney dysfunction (“rhabdomyolysis”) • Heart failure

RARE, AND SERIOUS In 100 people receiving trabectedin, 3 or fewer may have:
• Cough • Numbness, tingling or pain in the arms and/or legs (peripheral neuropathy) • Liver failure

Additional Drug Risks

The study drugs could interact with other drugs including prescription medications, over-the-counter medications, and herbal products. Your study doctor will give you a clinical trial wallet card that lists the study drugs. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.

- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

For women: Do not get pregnant or breastfeed while taking part in this study. **For all:** Tell your study doctor right away if you think that you have become pregnant during the study or within 3 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your uterine leiomyosarcoma. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the temozolomide, pazopanib or trabectedin (if applicable) ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- Blood that is drawn for research testing.

You or your insurance provider will not have to pay for the olaparib (if applicable) while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any drug company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research including the Imaging and Radiation Oncology Core (IROC).

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Where can I get more information?

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).

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 can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results may help other people with cancer in the future. The results will not be added to your medical records and you and your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but

cannot complete any of these optional studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, blood samples and leftover tissue from a previous biopsy will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Alliance for Clinical Trials in Oncology and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may be passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. About 2 tablespoons of blood will be collected from a vein in your arm four times during this study: before treatment begins, at the start of the second cycle, at the start of the fifth cycle, and after you stop treatment.
2. A sample from the tissue that was collected or biopsied in the past will be sent to the Biobank. Only leftover tissue will be stored. No new biopsies will be performed.
3. Your blood and tissue samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
4. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
5. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance.

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature