Title: A study of serum folate levels in patients treated with Olaparib

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RUSH

CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

Site Principal Investigator: Lydia Usha, MD

Address and Contact Information: 1725 W. Harrison Street, Suite 809, Chicago IL 60612
Clinic 24-hr phone: 312-226-2371

Protocol Title: A Study of Serum Folate in Patients Treated with Olaparib
Funder (s): AstraZeneca

Name of Participant: _____

Key Information:

You are being invited to participate in a research study. Research studies answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this research study is voluntary. You do not have to participate in this study and may choose to leave the study at any time. If you decide not to participate in this study or leave the study at a later time, your health care, benefits, or relationship with Rush University Medical Center will not change or be affected.

The purpose of this study is to learn more about olaparib-induced folic acid deficiency and to determine whether adding folic acid supplements might help prevent or treat the decrease in blood counts that can happen when patients take olaparib.

If you agree to participate in this study, your participation may last until you stop taking olaparib and you will be asked to come to the clinic every 2 weeks for the first 3 months. After that, you will come one time every month for study visits.

During these visits, you will be asked to give a blood sample and answer health questions. For a detailed list of study procedures, please see the "*What are the activities you will be doing if you participate in this study?*" section of this consent form.

There are risks to you for participating in this study. Folic acid, when given at the standard dose you will be receiving is well tolerated with no anticipated side effects. In this study, there is a risk of low blood counts, rash, and fever associated with olaparib. For a detailed list of risks you should know about, please see the "*What are the risks and discomforts of participating in this study?*" section of this consent form.

You may not directly benefit from taking part in this study, but we hope that knowledge gained from this study may benefit others with ovarian or breast cancer in the future.
You have the option to not participate in this study.

Detailed Information: Please review the rest of this document for details about the above topics and additional information you should know before making a decision about whether or not you will participate in this study.

Why are you being invited to participate in this study?

Your oncologist (cancer doctor) has recommended treatment with olaparib, (Lynparza™), which is a pill taken by mouth for advanced ovarian and breast cancers. It is an FDA-approved drug to treat certain types of cancers. We know that most patients tolerate olaparib fairly well based on published clinical studies. One of the common side effects is a decrease in blood counts, including red blood cells (anemia), white blood cells (leukopenia), and platelets (thrombocytopenia). The drug manufacturer recommends testing blood counts every month while on olaparib. If your blood counts drop, your doctor may need to decrease your dose of olaparib or to stop the drug entirely. It is not well understood why olaparib causes blood counts to drop. In a previous small study, 66% of subjects developed folic acid deficiency (low folic acid levels in the blood) within weeks of treatment with olaparib. Folic acid is a vitamin necessary for blood cell production, and reduced folic acid levels can cause a decrease in blood counts. Folic acid pills (supplements) were given to a small group of olaparib-treated subjects who developed anemia and folic acid deficiency. Their anemia improved, but it could not be determined if the added folic acid caused the improvement. You are being asked to take part in this study because we would like to learn more about olaparib-induced folic acid deficiency and to determine whether adding folic acid supplements might help prevent or treat the decrease in blood counts that can happen when patients take olaparib.

What is the purpose of this study?

The purpose of this study is to answer the following questions:

- What percentage of subjects develop folic acid deficiency after starting treatment with olaparib?
- How quickly does anemia develop after starting olaparib?
- For subjects who develop folic acid deficiency while on olaparib, does folic acid supplementation improve anemia, decrease the need for blood transfusions and allow subjects to stay on olaparib without needing to receive a smaller dose or stopping treatment?
- Does folic acid deficiency and folic acid supplementation impact the cancer response to olaparib?
- Why does folic acid deficiency occur in subjects treated with olaparib?

How many study subjects are expected to take part in the study?

Approximately 60 subjects will take part at Rush University Medical Center. Additional sites are likely to join after this study begins at this study site.

What will you be asked to do?

Once your oncologist determines that you need treatment with olaparib, you will first sign this consent form and then undergo a screening process to check eligibility for this study prior to starting treatment, which will include a routine blood sample to evaluate your baseline (starting) blood counts and folic acid levels**.** If you are eligible to participate**,** you will begin taking olaparib at the recommended dose **(**twice daily).

For the first 3 months, you will come to the clinic every 2 weeks for laboratory testing while on therapy. You will be asked to provide a blood sample (2 tubes, or about 2 tbsp.) to assess your blood counts and folic acid level.

Following this, blood samples will be required once a month for as long as you are on olaparib therapy. If you are found to have folic acid deficiency at any time during the first 3 months of therapy, a repeat blood test will be drawn in 2 weeks or at your next appointment. If a folic acid deficiency is confirmed and your Hemoglobin is ≥ 8 g/dL, you will be randomized to receive either oral (taken by mouth) folic acid supplement at 1 mg daily or no supplement. "Randomized" means you will have a 50/50 chance (like the flip of a coin) of getting either the folic acid supplement or no supplement.

You will have weekly blood draws to monitor your blood counts, folic acid level and potential need for transfusions. If you develop folic acid deficiency and your Hemoglobin is < 8 g/dL, you will start folic acid supplementation at 1 mg daily even if you were previously assigned to receive no supplement. Throughout the study, you will continue to follow up with your oncologist at regular clinic appointments. If at any time your oncologist believes you should no longer be treated with olaparib, you will be taken off the study 30 days after stopping olaparib, at which time a final sample of your blood will be drawn for folic acid levels and blood counts.

As an optional sub-study, we also will ask for your consent to access previously stored samples of your tumor for additional analysis. If you decide not to participate in the tissue sample portion of the study, you can still participate in the main study.

Does this study involve tissue/blood banking?

No, it does not.

Does this study involve genetic testing?

No, this study will not involve genetic testing.

What do you need to know regarding the collection of biospecimens?

Biospecimens may include blood, tissue, urine, bone marrow, saliva, cells, etc. In this study we will be collecting blood and leftover tumor tissue (optional).

If you agree to participate in the optional sub-study, leftover tumor tissue samples may be used for additional research in the future. The samples will be not be used for commercial profit and will not be sold. Results from the blood and tissue sample testing will not be shared with you. De-identified results may be published in medical journals. Most biospecimens contain DNA. We will not use biospecimens collected as a part of this study for whole genome sequencing, which involves mapping (identifying the location of genes and the distance between them) of all of your DNA.

Will your information or biospecimens be used for research in the future?

Information or biospecimens collected from you for this study may be used for future research or shared with other researchers. If this happens, information which could identify you will be removed before any information or biospecimens are shared. Since identifying information will be removed, you will not be asked for additional consent.

What if there is new information that may affect your decision to participate in this study?

During this study, you will be told about important findings (either good or bad), such as changes in the risks or benefits of participation in the study or new choices to participation that might cause you to change your mind about being in the study. If new information is shared with you, you may be asked to sign a revised consent form in order to continue participating in this study.

How long will you be in the study?

You will remain in the study for as long as you are treated with olaparib, as determined by your oncologist.

You may be removed from this study without your consent. Possible reasons may be that the study doctor decides that continued participation in the study will be harmful to you, you will need a treatment not allowed on the study, your disease becomes worse, you are unable to take the treatment as directed, or the study is canceled.

What are the possible risks of the study?

You are taking olaparib as the standard of care drug treatment. You may develop side effects from this medication. The risk for side effects are **not** increased by participation in this study. You should tell the study doctor about any side effects that you develop.

The most common side effects seen in more than or equal to 10% of subjects include:

- Swelling
- Tiredness
- Headache
- Dizziness
- Nausea
- Abdominal pain
- Vomiting
- Diarrhea
- Constipation
- Change in taste
- Decreased appetite
- Muscle pain
- Respiratory infection
- Low white blood cell count (cells that help fight infection)
- Low red blood cell count, also known as anemia which may make you feel tired or short of breath
- Low platelet count (cells that help blood to clot)

The most common side effects seen in 1 to 10% of subjects include:

- Rash
- Fever

Folic acid, when given at the standard dose you will be receiving is well tolerated with no anticipated side effects.

Frequent blood draws (up to once weekly if you have developed folic acid deficiency, detailed

above) may be inconvenient. During blood draws, you may experience pain or discomfort, and/or bleeding, and bruising at the site the needle enters the body, and in rare cases, fainting or infection.

Are there any anticipated pregnancy risks?

If you are pregnant or breastfeeding, you cannot receive treatment with olaparib and thus cannot be included in this study. A pregnancy test is required and will be given at the time of enrollment. You are responsible for using an effective birth control method such as birth control pills, barrier method (such as condoms or diaphragms), intrauterine device (IUD), hormone implants or surgical sterility while you are taking part in this study. If you become pregnant, you must notify the study doctor immediately.

Are there benefits to taking part in the study?

There may be no direct benefit to you for participating in this study**.**

Early detection of folic acid deficiency may improve the tolerability and safety of olaparib, allowing you to stay on the drug at the desired dose for a longer period of time. This in turn may lead to a better and more long-lasting response to treatment. In addition, you may be able to avoid blood transfusions on olaparib which could be otherwise necessary.

What other options are there?

The only alternative to participating in this study is not to participate.

What about confidentiality of your information

Records of participation in this research study will be maintained and kept confidential as required by law**.** Information regarding this trial will be shared with the funder of this study AstraZeneca Pharmaceuticals LP and its Affiliates are located around the world as well as companies who work for AstraZeneca who also may be located around the world, Food and Drug Administration (FDA) and the National Institutes of Health (NIH).

If you withdraw from this study, the data already collected from you may not be removed from the study records. The study doctor and/or study team may ask you whether they can continue to collect follow-up data on you.

Your identity will not be revealed on any report, publication, or at scientific meetings.
In order to conduct the study, the study doctor, Dr. Lydia Usha, and their study staff will use and share personal health information about you. This includes information already in your medical record, as well as information created or collected during the study. Examples of the information that may be shared include your medical history, physical exam and laboratory test results. The study doctor will use this information about you to complete this research.

Confidentiality and disclosure of your personal information is further described in the attachment to this form. The attachment is titled HIPAA Authorization to Share Personal Health Information in Research (2 pages).

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews new and ongoing human research studies to check that the rules and regulations are followed regarding the protection of the rights and welfare of human subjects.

What are the costs of your participation in this study?

All costs that are part of your usual medical care, such as blood counts and chemistry laboratory tests, will be charged to you or your insurance company. The folic acid supplements and the serum pregnancy, leutinizing hormone (LH), and follicle stimulating hormone (FSH) tests required for women of child-bearing potential at screening and at the first study visit will be provided to you free of charge.

You will be responsible for all costs that are not paid by your insurance company. You should check with your insurance company before you enroll in this research study.

Will you be compensated or paid?

No. Subjects will not receive compensation for their participation on this study. Your participation in this research study may contribute to the development of commercial products from which the funder company (AstraZeneca) or others may derive economic benefit. You will have no rights to any products, patents or discoveries arising from this research, and you will receive no economic benefit.

What happens if you experience a research related injury?

If you get ill or injured from being in the study, Rush University Medical Center will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact Dr. Usha at 312-226-237.

You should let any health care provider who treats you know that you are in this study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact your study doctor.

You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. Costs not covered by insurance could be substantial.

Rush University Medical Center has no program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

By signing this form, you are not giving up any legal rights to seek compensation of injury.

What happens if you need emergency care?

If you need emergency care while you are participating in this study, it is important that you tell emergency personnel of your participation in this study and notify the study doctor as soon as possible.

Whom do you call if you have questions or problems?

Questions are encouraged. If there are any questions about this research study or if you experience a research related injury, please contact Dr. Lydia Usha at 312-226-2371. Questions about the rights of research subjects may be addressed to the Rush Research & Clinical Trials Administration Office at 1-800-876-0772.

☐ I **agree** to participate in the optional sub-study and allow Rush University Medical Center to access previously-stored samples of my tumor for additional testing and analysis

☐ I **do not agree** to participate in the optional sub-study and allow Rush University Medical Center to access previously-stored samples of my tumor for additional testing and analysis

SIGNATURE BY THE PARTICIPANT:
By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study staff. You do not waive any of your legal rights by signing this consent/authorization form. You will be given a signed copy of this document.

_____	_____	_____
Name of Participant	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this consent document have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant.

_____	_____
Signature of Individual Obtaining Consent	Date of Signature

SIGNATURE BY WITNESS/INTERPRETER:
I observed the signing of this consent document and attest that, to the best of my knowledge, the person signing the consent form is the participant and the person signing the form has done so voluntarily.

_____
Name of Witness/Interpreter

_____	_____
Signature of Witness/Interpreter	Date of Signature