Cancer Center Research and Trials
Office
1520 W. Harrison St., RAB 3rd Floor
Chicago, IL 60607

RUSH

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COVER SHEET

TITLE: A study of serum folate levels in patients with solid tumors treated with Olaparib -ES 18-13807

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INFORMED CONSENT DOCUMENT

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RUSH

CONSENT/AUTHORIZATION 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 up to one year 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. Blood tests may be more frequent if you have low folate or low red blood cell levels in your blood.

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 solid tumor cancers 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 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 may 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. This 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).

You will come to the clinic for laboratory testing while taking olaparib, every 2 weeks for the first 3 months and then monthly for a total of 6-12 months. You will be asked to provide a blood sample (2 tubes, or about 2 tbsp.) to assess your blood counts and folic acid level.

If you are found to have folic acid deficiency at any time during the first 3-6 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 between 10-12 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 blood draws every 2 weeks unless your Hemoglobin is less than 10 g/dl, in which case you may need to have blood drawn weekly.

If you develop folic acid deficiency and your Hemoglobin is less than 10 g/dL, you will start folic acid supplementation at 1 mg daily even if you were previously assigned to receive no supplement. If you have been on Folic acid supplementation at 1 mg, and your Hemoglobin is less than 10 g/dl, then the folic acid supplementation will be increased to 2mg. You will then have weekly blood draws to monitor your blood counts, folic acid level, and the potential need for blood transfusions until your Hemoglobin is above 10 g/dl. Blood draws will then return to every 2 weeks.

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. Thirty days after stopping olaparib a final sample of your blood will be drawn for folic acid levels and blood counts.

As an optional sub-study, we will also ask for your consent to access previously stored samples of your tumor tissue from your initial cancer surgery or tumor biopsy that the cancer diagnosis was made on. The purpose of this consent is for future analysis of folate receptors or other tests still to be developed. The samples will be tested to help us answer the study questions, and any leftover samples may be used to develop new cancer tests, treatments, or tested to help us understand more about the disease and its characteristics. Frequently, biomarker data are generated towards the end of the study. Results from any of the additional tests will not be made known unless specifically requested. Samples will be kept for up to 10 years from your last visit and any leftover tissue will be destroyed. 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).

We will check your blood samples for the folate levels and other tests approved for the work-up of anemia (decreased Hemoglobin). We will not be storing any leftover blood samples.

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.

If you agree to participate in the optional sub-study, leftover tumor tissue samples will be collected and may be used for additional research in the future (as described above). The samples will be not be used for commercial profit and will not be sold. Results from the tissue sample testing will not be shared with you. De-identified results may be published in medical journals. Tissue samples will be stored for a maximum of 10 years from the date of your last study visit, after which they will be destroyed.

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 up to 12 months if you are receiving folic acid supplementation. If you do not receive folic acid supplementation, your participation will be complete at 6 months.

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. Your cancer treatment doctor will explain the risks associated with the drug. You can also find out more about the side effects of this drug online from the maker of this drug at https://www.lynparza.com/side-effects.html. The package insert which describes the usage of the drug and the side effects can be found in the FDA database at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208558s014lbl.pdf .

You should tell your cancer treatment doctor and the study doctor or nurse about any side effects that you develop.

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

This authorization is voluntary. Rush University Medical Center and its affiliates ("Rush") will not withhold or refuse your treatment, payment, enrollment, or eligibility for benefits if you do not sign this authorization. You do not have to sign this authorization, but that means that you cannot be in the study or receive study-related treatment.

By signing this document, you voluntarily authorize (give permission to) Dr. Usha, the study team, and other Rush personnel involved with the conduct and review of this study (which may include off-site personnel) to use or disclose (release) health information that identifies you for the study described in this document.

During the study, Dr. Usha and the study team will collect Protected Health Information (PHI) about you for the purposes of this research. PHI is your health information that includes your medical history and new information obtained as a result of this study. Some of this information will come from your medical record. The health information that Rush may use or disclose for this research includes: your medical history, physical exam and laboratory test results.

Dr. Usha and the study team may share your health information and the results of your study-related procedures and tests with people outside of Rush who assist with the conduct and review of this study. The persons who receive your health information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, but only if permitted by the laws governing them. Your health information described above may be used or disclosed to:

- To the Researchers
- The study Sponsor, AstraZeneca Pharmaceuticals, and its representatives and affiliates
- Monitoring agencies such as the Food and Drug Administration (FDA), the National Institutes of Health and the Rush Institutional Review Board (IRB).

While you participate in the study you will have access to your medical record, but Dr. Usha is not required to release to you study information that is not part of your medical record. Rush is required by law to protect your health information, and study records that identify you will be kept confidential. Any study information in your medical record will be kept indefinitely. Your identity will not be revealed on any report, publication, or at scientific meetings.

You have a right to inspect and copy the information to be disclosed with this authorization and you may obtain a copy of the information by contacting the office listed below.

If you no longer want to be in the study and do not want your future health information to be used, you may change your mind and revoke (take back) this authorization at any time by writing to Dr. Usha at 1725 W. Harrison Street, Suite 809, Chicago IL 60612. If the authorization is revoked, you will no longer be allowed to participate in the study and previously authorized individuals/entities may still use or disclose health information that they have already obtained about you as necessary to maintain the integrity or reliability of the current study.

This authorization is valid for the entirety of this research study. It will expire upon completion of the study or if you revoke (take back) the authorization.

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. If follow-up information will be requested, you will be asked to sign a separate consent form before this information can be collected.

Records of participation in this study will be maintained and kept confidential as required by law.

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. Screening blood tests, including 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. Additionally, blood work for research purposes only such as the twice weekly blood counts, chemistry panel, and folate levels done for the first 3 months, will be provided free of charge. If you develop folate deficiency, it is the standard of care to monitor folic acid levels, blood counts, and use blood tests to rule out other causes of anemia. These tests will be billed to your insurance.

Because it is important that all patients who need folic acid supplementation use the same dosage and brand, the folic acid supplements will be provided 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 312-226-2371.

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.

Investigator Financial Disclosure

This research study is supported by money from AstraZeneca. Dr. Dewdney (an investigator on this study) receives extra money from AstraZeneca for activities that are not a part of the study. The activities are for consulting and being on an advisory board for AstraZeneca. It was determined that the relationships are considered unlikely to affect your safety and/or the scientific quality of the study. This decision was given to the IRB for its review and approval of the study. If you would like more information, please contact Dr. Dewdney.

This research study is supported by money from AstraZeneca, LP. Dr. Fidler (an investigator on this study) receives extra money from AstraZeneca, LP for activities that are not a part of the study. The activities are for consulting for AstraZeneca, LP. It was determined that the relationships are considered unlikely to affect your safety and/or the scientific quality of the study. This decision was given to the IRB for its review and approval of the study. If you would like more information, please contact Dr. Fidler.

This research study is supported by money from AstraZeneca, LP. Dr. Rao (an investigator on this study) receives extra money from AstraZeneca, LP for activities that are not a part of the study. The activities are for, providing educational presentations and being on the scientific advisory committee for AstraZeneca, LP. It was determined that the relationships are considered unlikely to affect your safety and/or the scientific quality of the study. This decision was given to the IRB for its review and approval of the study. If you would like more information, please contact Dr. Rao.

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.

Consent for Optional Biomarker Sub-Study

☐ 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 future tumor testing and analysis for additional tumor markers for the development of new drugs, markers for determining prognosis, and folate levels.

☐ 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 future testing and analysis for additional tumor markers for the development of new drugs, markers for determining prognosis, and folate levels.

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

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AUTHORIZATION TO SHARE PERSONAL HEALTH INFORMATION IN RESEARCH

Name of the Research Study: A Study of Serum Folate in Patients Treated with Olaparib

Name of Principal Investigators: Jamile Shammo, MD and Lydia Usha, MD

The word "you" means both the person who takes part in the research, and the person who gives permission to be in the research. The word "we" refers to Rush University Medical Center, its employees and affiliates, including the study doctor and his/her research staff. You will be asked to sign this form along with the attached research consent form.

We are asking you to take part in the research described in the attached consent form. To do this research, we need to collect health information that identifies you. Some of this information may come from results of tests, procedures, questionnaires and interviews. We may also collect information from your medical record. We will only collect information that is needed for the research. This information is described in the attached consent form.

If you sign this form, we will collect your health information until the end of the research. We may collect some information from your medical records even after your direct participation in the research project ends. We may keep the information forever, in case we need to look at it again for this research study.

Your information may also be useful for other studies. We can only use your information again if a special committee in the hospital gives us permission. This committee may ask us to talk to you again before doing the research. But the committee may also let us do the research without talking to you again if we keep your health information private.

If you sign this form, you are giving us permission to collect, use, and share your health information.

You do not have to sign this form. If you decide to NOT sign this form, you cannot be in the research study. We cannot do the research if we cannot collect, use and share your health information.

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to the researcher listed above. The letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. If we cannot collect and share your health information, we may decide that you cannot continue to be part of the study. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

If you sign this form, we may continue to share the health information collected for this study with the people listed in the Confidentiality section, without any time limit, unless you withdraw your authorization. This authorization does not expire.

CONFIDENTIALITY

We may share your information with people who help with the research. Some of these people may be other researchers outside of the hospital or are in charge of the research, pay for or work with us on the research. Some of these people make sure we do the research properly. Some of these people may share your information with someone else. If they do, the same laws that Rush must obey may not protect your health information. For this study, we will share information with:

- Federal and state agencies (such as the Department of Health and Human Services and other government bodies that oversee or review research)
- The study Sponsor, its current or future research partners, collaborators, assignees, licensees or designees AstraZeneca AB and their affiliates, agents, and employees
- Health care providers who provide services to you in connection with this study
- Other individuals and organizations that analyze your health information in connection with this study, such as laboratories and other study sites participating in this study

If your information is transferred outside of the United States, different privacy laws may apply. Additionally, if one of the companies or institutions listed above merges with, or is purchased by, another company or institution, this authorization to use and disclose protected health information in the research will extend to the successor company or institution.

If you have any questions, please ask the researcher or his/her staff. Their phone numbers appear in the attached consent form. You can also call 1-800-876-0772 at Rush with general questions about your rights and the research use of your health information. The researcher will give you a signed copy of this form.

SIGNATURE, DATE, AND IDENTITY OF PERSON SIGNING

The health information about _____ can be collected and used by the researchers and staff for the research study described in this form and the attached consent form.

Signature: _____ Date: _____

Print name: _____ Legal authority: _____