SCREENING CONSENT FORM FOR RESEARCH: HRD Testing

Study title: IIT2015-18-Mita-MK3475: Open Label, Phase II Pilot Study of Immune Checkpoint Inhibition with Pembrolizumab in Combination with PARP Inhibition with Olaparib in Advanced BRCA-mutated or HDR-defect Breast Cancers

Study support provided by: MERCK & CO.

Cedars-Sinai Principal Investigator: Yuan Yuan, MD

Study contact phone number at Cedars-Sinai: 310-423-8255

This research study is sponsored by Merck. Merck only reimburses Cedars-Sinai Medical Center for the costs associated with running the study; Merck is not providing additional compensation to Cedars Sinai Medical Center or the Investigators for their participation in the study.

Please take time to read this entire form. You should ask questions before deciding whether to take part in this study. You can talk with family, friends and/or healthcare providers before you decide.

1. Purpose of the Study

You have been asked to take part in a clinical trial for patients diagnosed with a BRCA-mutated or HDR-defect breast cancer that has progressed (worsened) after previous treatment. There are two BRCA genes, BRCA1 and BRCA2, and they play a role in protecting cells from cancer. If one of these genes is mutated, cells may rapidly change and divide, which can lead to cancer. HDR-defect is another type of gene mutation that can contribute to development and progression of cancer.

Tempus HRD will be used to determine HDR status, for patients who do not otherwise qualify for the study based on BRCA status.

Before fully screening to participate in the treatment portion of the study, researchers would like to look at your tumor tissues that have previously been taken by either biopsy or surgery in addition to a blood or saliva sample. Researchers want to gather information from your samples to find out if you have the right type of cancer to take part in the study. This is called “screening”. In order to participate in the treatment portion of the study you must agree to have your tissue and blood/saliva screened.

The main research study is designed to test the investigational use of pembrolizumab and olaparib in breast cancer. Pembrolizumab, also known as KEYTRUDA, is approved by the U.S. Food and Drug Administration (FDA) for the treatment of a type of lung and skin cancer. However, it is not approved by the FDA for the treatment of breast cancer. Olaparib, also known as LYNPARZA, is approved by the U.S. Food and Drug Administration for the treatment of advanced BRCA-mutated HER-2 negative breast cancer. However, it is not approved by the FDA to be used in combination with Pembrolizumab for the treatment of breast cancer. Olaparib is also not approved by the FDA for the treatment of HDR-defect breast cancer.

Pembrolizumab is a drug that works with your immune system to target your tumor. Olaparib is also a drug that targets your tumor. We want to know if pembrolizumab and olaparib together will be able to reduce the size and amount of your cancer cells with fewer side effects than standard treatment by targeting your tumor.

The study will include up to 20 people in total.

Your direct participation in this screening will be done once the testing on your samples is completed.

2. Main Study Procedures

If you choose to be screened for the research study, a piece of your previously collected tumor tissue (archived tumor sample) from the most recent biopsy or surgery for your cancer will be collected. In addition, a blood sample (approximately 2 teaspoons) or saliva sample will be collected. The samples will be collected solely for research purposes. The samples collected would otherwise not be taken if you did not participate in this research study. No new tissue will be taken for this part of screening for the study.

Information about you including demographics, diagnosis, treatment and laboratory results related to your cancer will be sent with your samples as part of the HRD screening test. The information shared will not contain identifiable information that can be used to link you to your samples.

WILL I RECEIVE INFORMATION ABOUT MY SAMPLES?
The researchers will receive the results of these tests. The results will be shared with you but will not become part of your medical record. If you are willing and become eligible to take part in the treatment portion of this study the results will be included in your research records.

3. Possible Risks and Discomforts of the Main Research Procedures

This section talks about the possible risks and/or discomforts of the study procedures.

Risks of common medical procedures performed for research purposes are described below in Section 5. Side effects and risks of standard of care procedures are not described in this consent form.

Risks of Tempus HRD testing

In this study, archival tumor tissue samples as well as a normal matched sample (blood preferred, tissue, or saliva) may be collected for genetic testing, which may be used to determine your eligibility to participate in this study. In addition to your samples, de-identified clinical data elements will be shared with Tempus, the company performing the testing. Genetic studies have raised concern as to whether the studies would place research subjects at risk for discrimination based on genetics. The federal Genetic Information Nondiscrimination Act (GINA) was passed to address this concern. GINA makes it illegal for medical insurance companies and most employers to discriminate based on genetic information. The protections of GINA do not apply to life, disability, or long-term-care insurance. Although there are substantial protections against the risk of discrimination, you should be aware of this general concern. We follow federal and state privacy laws to protect against unauthorized disclosure of your protected health information that could lead to discrimination or the misuse of your genetic information.

4. Common Medical Procedures Performed for Research Purposes and Risks

The procedures listed below are often part of routine care for a person with your condition. They are not experimental procedures. The procedures and their risks are research-related. This means they are being *repeated* or performed *more frequently* for this study. These common procedures and their risks should be the same as when performed outside this study.

Study Procedure	Related Risks
Blood Draw: A needle is placed in the vein in your arm to draw blood. We will draw about 8mls one time for HRD screening.	Blood drawing may cause some pain. There is a small risk of bleeding, bruising or infection at the site of the blood draw. There is also a small risk of fainting.

5. Benefits From Taking Part in the Study

You should not expect to benefit from taking part in this screening study.

6. Whether Research Results Will Be Shared

A. ***Research Labs****:* All the research tests done in this study follow standard clinical procedures. They are performed in certified clinical labs. These test results may be shared with you. They may be placed in your Cedars-Sinai medical record.

Unanticipated Incidental Findings

We will contact you using the last contact information you gave if, unexpectedly, we find results that suggest potentially clinically relevant medical information. We may suggest you talk with your treating physician about possible additional clinical testing to further evaluate the

research finding. You and/or your insurance would pay for any additional testing and any related treatment.

7. Reasons Participation May Be Stopped

Your participation in this study may be stopped at any time. The researcher or the sponsor can stop your participation without your consent for any reason. Some reasons for stopping your participation include:

- The study is stopped or suspended.
- Funding for the study is reduced, stopped or withdrawn.
- It is in your best interest.
- You do not follow the study procedures.

8. Choosing to Take Part and Other Options

Taking part in research is voluntary. You have the right to choose not to take part. You can stop taking part in this research study at any time. You can do this without any penalty or loss of benefits to which you would be entitled outside of the study. Your choice not to take part or to stop taking part will not affect the care you get at Cedars-Sinai.

If you decide to stop taking part, we will keep any data collected on you up to the time you choose to stop. Also, if you stop taking part, the study team may ask you whether you want to give further data from your routine medical care.

9. Confidentiality Protections

We will do our best to keep your personal information collected as part of this study private. But we cannot guarantee total privacy. We may put a copy of your research consent and authorization forms in your electronic medical record at Cedars-Sinai. Your personal information may be given out if required by law. Publications or presentations about this study at scientific meetings will not use your name and other identifiable personal information.

Organizations that may look at and/or copy your medical records for research oversight, quality assurance and data analysis include:

- Accrediting agencies (agencies that grant official certifications to educational institutions)
- Government and regulatory groups, such as the Food and Drug Administration (FDA) and Office for Human Research Protections (OHRP)
- The Institutional Review Board (IRB), which reviews research to protect people taking part in studies
- Safety monitors, which monitors the safety of individual participants and the overall safety of the study
- Companies that sponsor the study and authorized representatives of the sponsor

Attached to this consent form is an Authorization Form. It outlines with whom your information may be shared for this research and under what circumstances.

We might share your information and/or research samples collected in this study. It might be shared with other researchers at Cedars-Sinai, other academic institutions or third-party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

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

10. Research-Related Illness or Injury

We do not expect you will have any illness or injury from this research study. If you believe that you are ill or have been injured from this study, please contact the study team at the phone number listed on page 1 of this consent form.

11. Financial Considerations

Costs of Participation
You and your insurance company will not be charged for your participation in this screening study.

Payment

You will not be paid for taking part in this screening study.

You will not be paid for giving biological samples (e.g., blood, fluid, tissue) for this study. Once you give the samples for the research, you no longer have access to them. Cedars-Sinai or the Study Sponsor will own your donated samples. Researchers might use your samples to develop new products, tests or discoveries. These inventions may result in commercial profit for the researchers, Cedars-Sinai and other organizations. If this happens, you will not receive any financial benefits.

Financial Interest in the Research
The principal investigator and institution have no potential financial conflict of interest with this study.

12. Contact for Questions or Problems

Please contact the investigator for questions, problems or concerns about the research. Their contact information is on page 1 of this form.

You might have feedback, questions, problems, concerns or want to obtain more information about this study. If so, you can talk with someone who is not part of this study by contacting:

Cedars-Sinai Human Research Protection Program (HRPP)
Phone: 310-423-3783
Email: ResearchConcerns@cshs.org
Website: cedars-sinai.org/research/administration/office-of-research-compliance/review-board.html

The Cedars-Sinai HRPP protects the rights and welfare of research participants.

Experimental Subject's Bill of Rights

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

AUTHORIZATION FOR USE AND DISCLOSURE OF IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH

1. USE AND DISCLOSURE OF HEALTH INFORMATION

If you agree to this Authorization, you give permission to the Sponsor, Principal Investigator, other investigators and their research team described in the Consent Form for Research ("Research Team") to use or disclose your identifiable health information ("private information") for the research study titled "IIT2015-18-Mita-MK3475: Open Label, Phase II Pilot Study of Immune Checkpoint Inhibition with Pembrolizumab in Combination with PARP Inhibition with Olaparib in Advanced BRCA-mutated or HDR-defect Breast Cancers." which is described in the Consent Form for Research ("Consent Form") to which this Authorization is attached. In particular, you authorize the research team acting under the direction of the Principal Investigator to review your medical records and collect your private information from the following sources:

- ☒ Laboratory tests
- ☒ Pathology reports
- ☐ Imaging reports (e.g., x-rays or scans)
- ☐ Photographs or videos of your image
- ☒ Doctor/clinic records
- ☒ Hospital/medical records
- ☐ Mental health records
- ☐ Billing records

☒ Demographics, which may include age, gender identity, race, ethnicity, and/or sexual orientation

☐ Other tests or other types of medical information: N/A

2. WHO WILL HAVE ACCESS TO YOUR PRIVATE INFORMATION?

Your private information will be used by and/or shared with the Research Team.

In addition to the research team, if applicable, the following parties may receive your private information and inspect your records:

- The reviewing Institutional Review Boards and Cedars-Sinai offices with authority to oversee research compliance.
- U.S. government agencies, such as the Food and Drug Administration and the Department of Health and Human Services.

- Researchers at other organizations who are participating in this research study.
- The Study Sponsor, its business partners, and Cedars-Sinai's business partners for matters related to research study oversight, conduct of the research, data analysis, use of research results in product development, and payment or reimbursement.
- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, with the Sponsor and/or the FDA.

Cedars-Sinai takes steps to protect your private information when sharing it with the recipients described above. Though these steps and applicable law are meant to protect your private information, there is a risk that a recipient could share your private information without your permission.

3. WHEN WILL MY AUTHORIZATION EXPIRE?

By signing this document, you authorize the use and sharing of your private information until the end of the research study and any related optional sub-study you choose to participate in.

4. REVOKING AUTHORIZATION

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the research team may still use or disclose private information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to the Principal Investigator of the research study by writing to the Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd, Suite 1800, Los Angeles, Calif. 90048 and/or emailing to ResearchConcerns@cshs.org.

5. NOTICE OF RIGHTS AND OTHER INFORMATION

You do not have to agree to this Authorization, but if you do not agree, you may not participate in the research study. Cedars-Sinai may not condition (withhold or refuse) the provision of standard of care treatment for you on whether you agree to this Authorization.

If you agree to this Authorization, please sign on the appropriate signature line on the Signature Page. You will receive a copy of this Authorization.

Signature Page

Consent Form for Research and Authorization for Use and Disclosure of Identifiable Health Information (Research)

If you agree to take part in this screening study, you should sign and date on the signature lines below. You will be given a signed and dated copy of this form. This includes the "Experimental Subject's Bill of Rights," "Authorization for Use and Disclosure of Identifiable Health Information (Research)" and any optional sub-study descriptions, when applicable.

Signature by the Participant
Screening Research Study: *I agree to take part in the screening study described to me during the informed consent process and described in this informed consent form. My questions have been answered to my satisfaction.*

You will be given a signed and dated copy of this form.

Participant name (please print)	Signature	Date

Authorization for Use and Disclosure of Identifiable Health Information (Research): *I hereby agree that my identifiable health information may be used and/or disclosed in accordance with the "Authorization for Use and Disclosure of Identifiable Health Information (Research)."*

Participant name (please print)	Signature	Date

Signature by the Investigator
I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.

Investigator name (please print)	Signature	Date

Signature by the Interpreter/Witness
(Signature of an interpreter is only required when enrolling a non-English-speaking subject with the assistance of an interpreter and IRB-approved "short form" consent

processes. The witness may be any person who is conversant in both English and the language of the non-English-speaking subject, such as a certified hospital interpreter, study staff, a family member or other person. The witness signs the consent forms to confirm that the oral interpretation occurred.

Signature of a witness is required when an English-speaking subjects who has been determined to have capacity to consent is unable to read or physically sign the consent form, but choses to indicate via a "mark" or verbally that he/she agrees to participate. The witness signs the consent form to confirm that an oral consent process occurred and that the individual verbally consented to participate in the research.)

Interpreter/Witness name (please print)	Signature	Date