Catholic Health

April 23, 2024

Johnny Kao, MD
Department of Radiation Oncology
CC: Rachel Radigan

Re: Feasibility Trial of Darwin OncoTreat and OncoTarget Precision Medicine Testing to Improve Outcomes for Patients with Limited Metastatic Disease that Failed First-Line Systemic Therapy
IRB # 24-002

Approval date: March 13, 2024 (Conditional Approval; Full Board)
Date conditions of approval were met: April 19, 2024
Expiration date: March 13, 2025

Dear Dr. Kao,

The GSHMC IRB met on March 13, 2024 with a quorum present and reviewed the protocol listed above. The determination was for a conditional approval, pending minor directed revisions to the consent forms and clarifying information to the application. This letter is to confirm that these conditions have been met and approval to initiate the study is now granted. The IRB Protocol identification # is 24-002.

The consent form and Protocol are approved. Please be sure to use copies of the attached, stamped consent document when enrolling subjects.

If you have any questions regarding this decision please contact the IRB Office at 631-376-3093.

Sincerely yours,

Lara R. Rush

Lara R. Rush, IRB Coordinator
Institutional Review Board
LaraR.Rush@chsli.org

INFORMED CONSENT TO PARTICIPATE IN CLINICAL TRIAL

Study Title for Trial Participants: Testing a new precision medicine test Darwin OncoTarget and OncoTreat in combination with involved site radiation for patients with limited metastatic cancer

Official Study Title for Internet Search: Feasibility Trial of Darwin OncoTarget and OncoTreat Precision Medicine Testing to Improve Outcomes for Patients with Oligometastastes that Failed First-Line Systemic Therapy

Principal Investigator:

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What is the usual approach to my metastatic cancer?

You are being asked to take part in this study because you have metastatic cancer that can be treated with targeted radiation to all areas of visible involvement (up to 10 areas). You have already been treated with standard first-line systemic therapy. While some patients remain free of cancer with standard salvage therapy combined with radiation, approximately 70 to 80% of patients eventually recur. We are studying whether using a new precision medicine test can achieve better results.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may receive standard systemic therapy and/or radiation therapy as determined by your oncologists
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer except for comfort care to relieve symptoms

Why is this study being done?

The purpose of this study is to test the ability to use and carry out the precision medicine test called Darwin OncoTarget and OncoTreat. This study is assessing whether precision medicine recommendations will be used to change treatment choice compared to standard of care to in a community hospital setting, as well as if the treatment recommended will be accessible to

patients. While analyzing tumor DNA through genomic testing of advanced cancer is now common, this practice does not seem to improve survival for most patients. Researchers hope that newer precision medicine tests that go beyond DNA to include RNA sequencing and computer algorithms can better identify cancer's weak spots by identifying master regulators of uncontrolled cancer growth. Darwin OncoTarget and OncoTreat precision medicine tests are commercially available but have not been widely used to recommend systemic treatment as well as in combination with your radiation treatment. Since patients undergoing comprehensive involved site radiation have all their visible disease treated, we hypothesize that FDA-approved treatments recommended by this test could further reduce the probability of recurrence. There will be about 20 people taking part in this study.

What are the study groups?

All study participants will get the same study intervention. It will include the usual radiation to all areas of visible disease. Systemic therapy will be determined by your medical oncologist with the supplemental information provided by the Darwin OncoTarget and OncoTreat test.

We will perform a biopsy and send the tissue to Columbia Presbyterian Medical Center for Darwin OncoTarget and OncoTreat testing. It is possible that the biopsy is inadequate for testing, in which case you will not be eligible to continue in the study as treatment recommendations will not be able to be given. Darwin OncoTarget and OncoTreat will recommend FDA drug treatments based on identifying master regulators of your tumor. Your oncologist will either recommend standard systemic therapy or will utilize FDA approved treatments recommended by the Darwin OncoTarget and OncoTreat test.

How long will I be in this study?

You will be followed for 5 years with standard of care from your doctor that includes history, physical examination, toxicity monitoring and tumor imaging.

You will undergo standard treatment for limited metastatic cancer while being assessed with Darwin OncoTarget and OncoTreat testing. If your doctor decides to not use the results of the OncoTarget and OncoTreat testing, you will remain on standard treatment. If they decide to use OncoTarget and OncoTreat recommended therapy, your treatment regimen may be switched. Your doctor will follow your condition for up to 5 years to determine the impact of precision medicine testing on your treatment, side effects and overall outcome, regardless of if they decide to use the OncoTarget and OncoTreat recommendations.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests that you have if you take part in this study. These are: 1) A needle biopsy of your tumor tissue; 2) Darwin OncoTarget and OncoTreat testing. The biopsy will be sent for Darwin OncoTarget and OncoTreat testing, which will have a turnaround time of 21 days.

Before you begin the study:

A biopsy is a small piece of cancer tissue removed by a needle. Biopsies are often ordered by oncologists before changing treatment. For this precision medicine study, biopsy is necessary for optimal accuracy of the Darwin OncoTarget and OncoTreat recommendations.

Common side effects of a biopsy are a small amount of bleeding at the time of procedure, pain at the biopsy site, which can be treated with regular pain medications and bruising. Rarely, an infection can occur. You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the lists that links the code to your name will be kept separate from your sample and health information.

Since a tumor biopsy is considered standard of care and medically necessary to diagnose and treat cancer, your insurance carrier will be billed for this procedure. There is concern that health insurance plans may not cover all medically necessary diagnostic patient care costs associated with usual cancer care for patients enrolled on clinical trials. The National Cancer Institute has attempted to address this potential barrier to clinical trial enrollment at:

Cancer.gov/research/participate/clinical-trials/paying

Neither you nor your insurance carrier will be billed for Darwin OncoTarget and OncoTreat testing that will be used for your study.

A piece of your tissue sample will be used to Darwin OncoTarget and OncoTreat testing; the rest of your tissue sample will be stored per the guidelines of the Laboratory at Columbia Presbyterian Medical Center.

In addition to Darwin OncoTarget and OncoTreat testing, you will undergo standard examinations, tests and procedures for patients with metastatic cancer determined by your oncologists including history and physical examinations, blood tests, PET, CT or MRI testing. These are all part of your usual care.

The data points that will be shared from the pts medical records and the data protection plan and sharing plan must be outlined point by point for IC to occur.

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

Except for the biopsy, there are no risks inherent to precision medicine testing because this is simply analyzing the RNA from the tumor with a computer algorithm.

Risks associated with the biopsy are a small amount of bleeding at the time of procedure, pain at the biopsy site, bruising, and infection.

The turnaround time is currently 21 days so it is possible that your cancer and the treatment can progress during this time, and as a result your doctor will choose not to use the results in which case you do not benefit from testing. During these 21 days, you will be receiving standard treatment recommended by your oncologist.

Once the results are available, there are several possible risks:

There is a risk your oncologist will decide not to use these results. In that case, you will not benefit from this test.

It is possible that your research team will be unable to obtain the drugs recommended by the test because insurance declines to provide coverage and/or the research team is unable to obtain compassionate use administration from the drug company. In this scenario, you will receive standard systemic therapy recommended by your oncologist and will not benefit from this test.

It is possible that Darwin OncoTarget and OncoTreat recommends an FDA approved drug that does not work or causes side effects. Since we will not know the specific drugs recommended by Darwin OncoTarget and OncoTreat ahead of time, your oncologist will review potential side effects with you prior to starting treatment. Some of the FDA approved drugs recommended by Darwin OncoTarget and OncoTreat have not been used in patients who received radiation and therefore there can be unexpected side effects.

There is a risk of potential loss of data confidentiality in the case of a data breach. Your data will be tracked using the Electronic Medical Record system for regular follow-ups with your doctor for the 5 years that you will be enrolled in addition to the study specific data gathered. Any data breaches will be directly reported to the IRB.

What possible benefits can I expect from taking part in this study?

This study has only a small to moderate chance of helping you because Darwin OncoTarget and OncoTreat is still relatively new and we do not know if ordering this test and following its recommendations will improve outcomes compared to radiation with usual systemic therapy. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide

whether to let the study doctor continue providing your medical information to the organization running the study.

The 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.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the Good Samaritan University Hospital Institutional Review Board at 631-376-3093.

Where will my information be stored?

Confidentiality of your records will be maintained on a password protected computer with only necessary personnel having access to your information.

Your information collected as part of this study will not be used or distributed for future research studies.

What are the costs of taking part in this study?

Darwin OncoTarget and OncoTreat testing will be supplied at no charge while you take part in this study.

You and/or your insurance company will need to pay for all the costs of treating your cancer while in this study including the costs of tests, procedures or medicines to manage any side effects as part of standard cancer treatment. A biopsy is standard of care for your treatment and as such we expect it to be covered by insurance; however, if it is not, you will be responsible for coverage of costs. Since Darwin OncoTarget and OncoTreat recommended drugs are all FDA approved, we will attempt to obtain insurance coverage for recommended agents through the preauthorization process. If that is unsuccessful, we will attempt to obtain access to medications directly from the manufacturer through compassionate use. If insurance coverage cannot be obtained for Darwin recommended medications, your oncologist will utilize standard of care medication.

In the case of compassionate use medications, your insurance company may still be billed for services related to administration of treatment. Before you decide to be in the study, you should check with your insurance company to find out exactly what they will pay for.

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

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

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Although unlikely, it is possible that your insurance company may not be willing to pay for injuries related to Darwin OncoTarget and OncoTreat recommended FDA approved medications. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Where can I get more information?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov.

Who can answer my questions about this study?

You can talk to the study doctor about any questions and concerns you have about this study or to report side effects or injuries. Contact the study doctor Dr. Johnny Kao at 631-376-4047 or IRB Coordinator Lara Rush at 631-376-3093.

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 copy of this form. I agree to take part in this study

Print Name of Participant	Signature of Participant Date
Print Name of Person Obtaining Consent	Signature of Person Obtaining Consent Date