PRINCIPAL INVESTIGATOR: Alice P. Chen, M.D.

STUDY TITLE: A Phase I/II Trial of TRC102 (methoxyamine HCl) in Combination with Temozolomide in Patients with Relapsed Solid Tumors and Lymphomas

STUDY SITE: NIH Clinical Center

Cohort: Treatment

Consent Version: 7/6/2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent for themselves, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in this study. For the remainder of this document, the term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

We are doing this study to try to develop better treatments for cancer. An experimental drug, TRC102 will be given to you with temozolomide, which is a chemotherapy drug approved by the US Food and Drug Administration (FDA). The purpose of this study is to test the safety of TRC102 in combination with temozolomide and find out the dose of the drugs that can be safely given to humans. We are trying to understand how TRC102 works in humans, how your body handles this drug, what side effects the drugs cause, and the safety of the drugs at the given dose.

Temozolomide works by damaging the DNA of cancer cells to stop them from growing. TRC102 is thought to work by blocking repair of DNA damage induced by chemotherapy so that the chemotherapy works better. TRC102 is an experimental drug that has shown some anticancer effects against tumor cells in the laboratory and in experimental animals. This drug is in the beginning stages of being tested in humans.

We are also studying the genes in your tumor to help us understand how your tumor responds to TRC102 and temozolomide. Blood, tissue, and tumor cells contain genes that are made up of DNA and serve as the "instruction book" for each cell in the body. We know that variations in some tumor genes play an important role in how cancers respond to drugs. Determining whether different tumor gene variations affect how TRC102 and temozolomide work against tumors will help scientists understand which patients might respond best to these drugs.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this research study because you have non-small cell lung cancer, granulosa cell ovarian cancer, or metastatic colon carcinoma cancer that has progressed after receiving standard treatment, or for which no effective therapy exists.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 140 patients will take part in this study. As of May 2016, 47 patients have taken part in the "phase 1" part of the study to learn about the safety of the drugs and how TRC102 works in humans. The tumors in five of these patients got smaller, but did not go away. These patients had one of three types of cancer: non-small cell lung cancer, granulosa cell ovarian cancer, or metastatic colon carcinoma. To learn if patients with these three types of cancer are more likely to benefit from the study drugs, we changed the study design to look only at these patients. This is called the "phase 2" part of the trial.

DESCRIPTION OF RESEARCH STUDY

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

BEFORE YOU BEGIN THE STUDY

You will need to have the following examinations, tests, or procedures to find out if you can be in the study. These tests are part of your regular cancer care and should be done by your health care team even if you do not join the study. If you have had them recently, they may not need to be repeated. This will be up to your study doctor. Willingness to give blood and urine samples and have tumors biopsied for research is required for taking part in this study.

If you decide that you would like to participate in this study, you will be asked to sign this consent form. You will then have the examinations, tests, and procedures listed below done to see if you can take part in the study (this is called the screening/baseline evaluation).

- **Complete medical history.**
- **Physical examination,** including height, weight, blood pressure, pulse, and temperature.
- **Standard blood tests** (requiring about 1 tablespoon of blood in total), which include measurement of your white blood cells, red blood cells, platelets, and electrolytes, and how your liver and kidneys work.
- **Pregnancy test** in women who are able to become pregnant.
- **Urine tests:** Depending on the results of blood tests, you may be asked to collect your urine for further testing.
- **Electrocardiogram** to check your heart.
- **CT scans (a computerized x-ray examination)** or other imaging tests to measure your tumor(s).
- **Pathology slides:** Before starting on the study, we will request tumor slides or blocks to confirm your diagnosis.

DURING THE STUDY

If you are accepted and you choose to take part, you will begin receiving TRC102 and temozolomide. You will take temozolomide and TRC102 by mouth once a day, for 5 days. The drugs are given in cycles, and each cycle is 28 days (4 weeks) long. Each patient will receive the same dose, which was selected based on the side effects seen in the "phase 1" part of the study. Your dose of study drug may be decreased by the study doctor if you are not tolerating it well.

Both drugs will be provided as capsules and should be taken at the same time on an empty stomach, either 2 hours after a meal or 1 hour before a meal. Patients should drink a glass of water after taking TRC102 and temozolomide. TRC102 and temozolomide capsules should not be opened or

chewed. If the capsules are accidentally opened or damaged, care should be taken to avoid breathing in or touching the drugs.

You will be asked to maintain a diary to document the exact time you took the study drugs, and to report any side effects that you may have. If you miss a dose or vomit the dose, please make a note of this in your diary and contact your team immediately to receive further instructions. Please bring the study diary with you to each clinic visit.

You will also have tests and procedures done because you are in the study to see how TRC102 and temozolomide are affecting your body. This will include repeating some of the imaging studies (for example, CT scans, a computerized x-ray examination) to find out if your cancer has responded. Descriptions of the tests and procedures that will be performed during the study are listed below. Please see the Study Chart below for more details.

Clinical Center Visits: We will ask that you come to the Clinical Center once per week for the first three weeks of cycle 1; the week four visit may be performed by your home physician. Any findings by your home physician will be forwarded to the study doctor. We will then ask that you come to the Clinical Center for 1 or 2 days at the beginning of all other cycles. If you develop any side effects, you may be asked to visit more often.

TESTS AND PROCEDURES THAT ARE EITHER BEING TESTED IN THIS STUDY OR BEING DONE TO SEE HOW THE DRUG IS AFFECTING YOUR BODY:

- **Measurement of TRC102 in your blood:** We may collect blood samples to measure the amount of study drug in the blood and to help us find out how the body handles the drug. Blood will be collected at multiple time points during cycle 1 only. Please see the study chart for more details. The total blood for all these tests will be about 1~2 tablespoons.
- **Effect of TRC102 on your red blood cells:** One of the side effects of TRC012 is anemia (fewer than normal numbers of red blood cells in your blood). We would like to collect blood before and during the study to learn why some patients have anemia. This study is optional. The total amount of blood collected for this study will depend on what tests are done. Your study team will explain these tests in more detail.
- **Other research blood samples:** We will also be collecting optional blood samples to find out the effects of the drug on any tumor cells in your blood. Blood samples will be requested at the beginning of the study on cycle 1, day1. If you are having a tumor biopsy on day 4 or day 5, then blood samples will also be requested on that day. Blood samples will also be requested on day 1 of every cycle. Each of these blood collections will be about 1 teaspoon (4 mL). We will also collect an optional blood sample at the beginning of

the study (or as soon as possible) to find out whether the genetic features found in your tumor are also present in your blood; this blood collection will be about 1 teaspoon (5 mL).

- **Imaging scans**, such as CT scans, MRI, or ultrasound (an examination using sound waves), that detect your tumor will be done before the study and every 8 weeks (12 weeks if you have been on study more than 1 year) while you are receiving study drugs. This is done so that any benefit of the treatment can be determined, and if your cancer is not responding to the treatment, the study team can tell you and discuss other treatment options (discussed further below).
    - **Computed Tomography (CT) scan**: The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures showing the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan and you will be instructed to hold your breath. The scan itself will only take a few minutes to complete, the entire visit will take about 30 minutes
    - **Magnetic resonance imaging (MRI)**: An MRI creates pictures of the inside of your body using strong magnets instead of x-ray energy. At the time of each scan you will be asked to fill out a screening form to verify that it is safe for you to have the scan. You will also be asked to remove any metallic objects you may be wearing (for example, watches, earrings or piercings) and possibly to change into a hospital gown. Then you'll be asked to lie on a narrow bed that will move into the MRI scanner. Once you are comfortable, the table will be moved into the scanner (the scanner is a long, narrow tube that is open at each end). You will need to lie still on the table during the scan which will take about 60 minutes to complete. You will hear normal "hammering" or clicking and squealing noises during the scan. While in the scanner you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the technician running the scan the entire time and will be provided an emergency button to squeeze at any time if you decide you want the scan to stop.

      During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (IV) catheter. It will be done for both research and medical purposes.

      It is not known if MRI with contrast is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan with contrast. The scan will not be done if the pregnancy test is positive.

- **Tumor Biopsy:** After you are accepted to take part in the study, you will be asked to have imaging-directed biopsy of your tumor (removal of a small bit of tissue for microscopic examination) once before you receive the study drug and a second time a few days later (on Day 4 or Day 5). An optional biopsy may be requested later in the study.

- An **electrocardiogram** (ECG) is a test that is performed while you lie still for about 5 minutes. It involves placing electrodes (small stickers that are attached to wires that go to the machine) on the chest and arms/legs and recording the electrical activity of your heart. If you have a lot of hair on your chest, it may hurt a little bit when they remove these stickers.

We are collecting biopsy samples to study the effects of TRC102/temozolomide on your tumor and to search for any gene variations in your tumor that may help us understand how it responds to TRC102/temozolomide. Biopsies are an important part of this trial and are done for research purposes. Willingness to have tumor biopsies is required for taking part in this study for patients on the colon cancer and granulosa cell ovarian cancer cohorts; tumor biopsies are optional for patients on the NSCLC cohort. After the first biopsy, if you decide not to have further biopsies, you will still receive study drugs and have other tests that are part of the study.

If you are already taking part on this study and are tolerating the study drugs well, we may ask you for permission to obtain and use tumor tissue already collected from you before you started this study. We will use this tumor tissue for research to learn how your cancer is responding to the study drugs. We may also ask you to consider having a biopsy while you are on study. This biopsy is optional. No more than three biopsy procedures will be performed during the study.

You will be asked to sign a separate consent form for each biopsy procedure.

Tumor biopsies are only collected by trained personnel. Biopsies are collected using a needle under imaging guidance (CT, MRI, or ultrasound as deemed appropriate by the interventional radiologist performing the biopsy). Imaging helps the specialized radiologist know that the needle has been placed into the tumor mass.

Typical risks of biopsy collection include, but are not limited to, bleeding, infection, pain, and scarring. If you experience any complications from the biopsy, medical care will be offered to you. You will be counseled in more detail about biopsies, and you will be asked to sign a separate consent form that will describe the procedures and risks at that time. Your safety is the most important thing at all times. If upon attempting the first biopsy, no tissue can be obtained or it has caused you harm, further biopsies will not be done. After you are enrolled in this study, if for any reason the biopsies cannot be done safely, you may still receive the study drugs but the biopsies will not be done.

I agree to allow biopsies for research purposes:

Yes ____ No ____ Initials_____

GENOMIC SEQUENCING

We are also requesting your permission to perform exome sequencing on your tumor biopsies and blood and link this information to information from your medical history. You are not required to agree to exome sequencing to take part in this trial. Your blood and tumor tissue samples contain genes, which are made up of DNA (**d**eoxyribo**n**ucleic **a**cid) and serve as the "instruction book" for the cells that make up our bodies. Exome sequencing will determine the exact order of the base pairs (DNA building blocks) in your tumor and blood. This information combined with information from your medical history may help us understand how your tumor responds to TRC102 and temozolomide. We know that variations in some tumor genes play an important role in how cancers respond to drugs. Determining whether different tumor gene variations affect how TRC102 and temozolomide work against tumors will help scientists understand which patients might respond best to these drugs.

Tumor Sequencing

We will identify gene variants in your tumor biopsy samples collected before and during the first week of treatment with exome sequencing, but this information will be for research purposes only and we will not give you any individual results from this sequencing or add this information to your medical records. This is because it will probably take a long time for this project to produce health-related information that we will know how to interpret accurately. However, we will tell you if we find that you have a communicable disease that we are required by law to report.

If your disease starts to worsen and you choose to have a third, optional tumor biopsy, we may perform a more specific, targeted sequencing assay on this tumor tissue in a clinically approved laboratory. You and your doctor will receive the results of this test, and the results will be in your electronic medical record. Your doctor will discuss these results with you and any potential treatment options as a result of this test.

Germ Line Sequencing

To identify the gene variants in your tumor, we will need to compare them to the genes in your blood that you were born with (germ line sequencing). While looking for these changes, we may also find gene variants that increase a person's chances to develop a health problem. The types of gene changes we may find include:

- Changes in genes that are related to cancer.
- Changes in genes that are related to diseases other than cancer.

- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

These types of gene changes may or may not have a direct effect on you or your family members. It is important for you to know that everyone carries these types of gene changes and that we expect to find these types of changes in many of our participants. We will look for changes in genes that are important to you or your family's health one time, and if we find such changes the results will need to be confirmed in a clinical laboratory. If you want this to be done, we will draw an additional blood sample and send it for confirmatory testing. Once the results are available, if you would like to receive your results we will offer to have you come to NIH (at our expense) to have genetic education and counseling to explain this result. If you do not want to come to NIH, we will help you find a local genetic healthcare provider who can explain it to you (at your expense).

If you are not contacted about gene variants that might be related to a disease, that does not necessarily mean that all your genes are "normal". We are not able to detect all changes that affect the function of a gene with sequencing. This is one of the limitations of the testing that we will do.

- You will only be informed of genetic changes that researchers involved in this study feel are urgently important for your health or your family's health and that knowledge of these changes has the potential to provide a significant benefit for you or your family.
- You will not be told about all genetic changes including changes in genes that are not known to cause any disease, those variations that are of uncertain clinical importance, or results showing that you are a carrier of a single copy of a genetic variant when that is not enough to impact your health because your other copy of the gene has no variant.

If you have any questions about this information or would like to talk to one of the study's genetic healthcare professionals about the testing being performed on this study, please tell your doctor or contact Kathleen Calzone, 240-760-6178 or calzonek@mail.nih.gov.

I agree to allow genomic sequencing for research purposes:

Yes ____ No _____ Initials_____

STUDY CHART

The study drug is given over 28-day periods of time called cycles. You will take TRC102 and temozolomide by mouth on an empty stomach, either 1 hour before or 2 hours after a meal.

The chart below on the next page shows what will happen to you during cycle 1 and future cycles after you sign the consent form and start the study. Each cycle is numbered. The left-hand column shows the day in the cycle, and the right-hand column tells you what will happen on that day.

Day	What to do and what will happen to you
Before starting study drugs	• Check in at the Outpatient Clinic • Get routine blood tests and electrocardiogram of your heart • Pregnancy test for women who are able to become pregnant • Have a history taken and undergo a physical examination by a Health Care Provider • CT or MRI scan will be done • Tumor biopsies will be taken
Cycle 1, Days 1 and 2	• Admitted to the Clinical Center • Have a history taken of how you feel • Blood sample for research may be taken prior to taking the drug and 8 hours after taking the drug • Begin taking TRC102/temozolomide by mouth once a day • Blood samples for measurement of TRC102 (optional) may be taken at several times over 24-hours (before your first dose and 1, 2, 3, 4, 8, 12, and 24 hours after)
Cycle 1, Day 4 or 5 (if you are having a tumor biopsy)	• Blood sample for measurement of TRC102 may be taken before you take TRC102/temozolomide • Blood sample for research may be taken before taking the drugs • Tumor biopsies will be taken for some patients
Cycle 1, Day 8	• Routine blood tests will be done locally or at the Clinical Center
Cycle 1, Day 15	• Check in at the Outpatient Clinic for routine blood tests and a physical examination
Cycle 2, Day 1	• Check in at the Outpatient Clinic for routine blood tests, a history of how you feel, and a physical examination • Blood sample for research will be taken before taking the drugs

Day	What to do and what will happen to you
Cycle 3 and onwards, Day 1	• Check in at the Outpatient Clinic for routine blood tests, a history of how you feel, and a physical examination • CT scan to determine how your tumor is responding to the drugs will be done every 8 weeks (12 weeks if you have been on study more than 1 year)
Cycle 6 and onwards, Day 1	• One additional tumor biopsy may be taken for some patients if their disease shows signs of coming back

RISKS OR DISCOMFORTS OF PARTICIPATION

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer or condition 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 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 will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.

- 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.

The tables below show the most common and the 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.

The tables below show the most common and the most serious side effects that researchers know about. We learned during the "phase 1" part of this study that high doses of drugs caused anemia that required transfusion, so we chose a lower dose for this "phase 2" part. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Risks and side effects related to TRC102 may include:

POSSIBLE, SOME MAY BE SERIOUS
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Sores in mouth which may cause difficulty swallowing • Tiredness, fever • Loss of appetite • Itching, rash

Risks and side effects related to temozolomide may include:

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

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Temozolomide, from 4 to 20 may have:
• Headache, seizure • Infection, especially when white blood cell count is low • Anemia which may cause tiredness • Bruising, bleeding • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require blood transfusions

RARE, AND SERIOUS In 100 people receiving Temozolomide, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Cancer of bone marrow caused by chemotherapy • Rash • Severe skin rash with blisters and can involve inside of mouth and other parts of the body • Liver damage which may cause yellowing of eyes and skin, swelling and may result in liver failure.

Risks associated with genetic testing:

Privacy Risks

Your privacy is very important to us and we will use many safety measures to protect your privacy. Your research samples will be stored with a coded identifier, not your name. Any personal data about you will also be stored in a sequence computer database with that code

identifier. All information that can directly link you to the tissue or personal information will not be shared with investigators using your specimens for research. This includes information that contains your name, medical record number, date of birth, or address.

There are protections in place that restrict who can see the results of your genetic tests. However, there remains a risk someone could get unauthorized access or break into the system that stores information about you. Every precaution will be taken to minimize this risk. There also may be other privacy risks that we have not foreseen.

Genetic variant results that we return to you will become part of your medical record at the NIH. In spite of all of the safety measures that we will use, we cannot guarantee that your identity will never become known. For instance, if you or a family member releases information about you or your involvement in this study, or an insurer, employer, or other person obtains your written consent to receive information from your NIH medical record, your identity, information about your enrollment in this study and genetic variant results may be included in a release of your medical records.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

Emotional and psychological risks

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond. *A*lthough your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your testing results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Reproductive Risks:

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we do not know how TRC102/temozolomide would affect your baby or your unborn child. You should not become pregnant or father a baby while on this study and for 3 months after you stop taking the drug because the drugs in this study can affect an unborn baby. It is important you understand that you need to use birth control while on this study and for 3 months after the study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once. Patients who become pregnant while taking part in the study will be taken off the study.

Effective forms of birth control include:

- abstinence
- hormonal [birth control pills, injections, or implants]
- vasectomy
- intrauterine device (IUD)
- tubal ligation
- barrier methods(condoms)

Radiation Risks

During your participation in this research study, you will be exposed to radiation from CT scans. The amount of radiation exposure you will receive from these procedures is equal to approximately 10.1 rem per year. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scan that you get in this study will expose you to the roughly the same amount of radiation as 26 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 1.1 out of 100 (1.1%) and of getting a fatal cancer is 0.55 out of 100 (0.55%).

Risks for MRI

People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks for Gadolinium-Enhanced MRI

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)". This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA recently issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to

years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain.

Electrocardiogram Risks

Other than possibly experiencing some minor skin irritation from the electrodes there are no anticipated risks related to complete the electrocardiogram and/or the echocardiogram.

Blood Draw Risks

Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint. The study team member may apply numbing cream to the area so that the needle stick won't hurt as much.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to see if this experimental treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

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

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

RESEARCH SUBJECT'S RIGHTS

What are my rights if I take part in this study?
Taking part in this study is your choice. You may choose either to take part or not to take part in this study. If you decide to take part, you may leave the study at any time. No matter what decision you make, there will be no penalty to you, and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution if you are eligible and choose to participate in another trial. We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if too many patients in the study experience severe side effects
- if you become pregnant

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first. If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to the Cancer Therapy Evaluation Program (CTEP) at the National Cancer Institute (NCI) or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

FOLLOW-UP

You will be followed for at least 30 days after taking the last dose of study drugs. We will call you between days 27-30 to ask about any side effects that were ongoing when you stopped therapy, or any new side effects that might be related to the study therapy. If you have side effects that might be related to the study drugs that have not gotten better after 30 days, we will call you every 2 weeks until the side effects have become stable or gotten better. The follow-up period will end if you enroll in another study or start receiving standard therapy.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution but they do not need to report their personal finances to the NIH.
Tracon Pharmaceuticals, Inc. is providing one of the drugs for this study to NIH without charge. No NIH employee involved in this study receives any payment or other benefits from Tracon Pharmaceuticals, Inc.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

We would like to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be identified by a number and not your name. Your specimens and data will be used for research purposes only and will not benefit you. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you decide now that your specimens and data can be kept for research and shared, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research.

Please read the sentence below and think about your choice. After reading the sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

My specimens and data may be kept and shared for use in research to learn about, prevent, or treat cancer or other health problems.

Yes No Initials_____

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

The NCI Developmental Therapeutics Clinic will cover some or all of your travel expenses related to participation in this study. This may include direct payments or reimbursements for expenses related to transportation, lodging, and meals. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. We will give you a copy of this policy.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.

- National Institutes of Health Intramural Institutional Review Board
- The study sponsor, the NCI Cancer Treatment Evaluation Program, or their agent(s).
- Qualified representatives from Tracon, the pharmaceutical company who produces TRC102.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Alice P. Chen, chenali@mail.nih.gov, (240) 781-3320. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person

providing interpretive support is: _____.