To: CTEP Protocol and Information Office

From: Susanne Arnold, M.D.

Date: May 17, 2023

Re: Amendment #12 (Revision 15) for NCI Protocol #10388: "A Phase I Trial of Triapine and Lutetium Lu 177 Dotatate in Combination for Well-Differentiated Somatostatin Receptor-Positive Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)."

SUMMARY OF CHANGES
Consent Form (PVD 03MAY2023)

Changes by PI

#	*Section*	*Comments*
1	General	Version Date updated in header to match protocol version date.
2	What will happen if I decide to take part in this study?	The follow up duration has been clarified to state that patients will be followed up every 3 months from the time of enrollment for a total of 2 years. Patients removed from study for unacceptable adverse event(s) will be followed until resolution or stabilization of the adverse event.
3	Study Calendar	Clarify that follow up will be for 2 years from the time of enrollment.

Comments Requiring a Response– Administrative & Editorial Issues:

#	*Section*	*Comments*
1.	What exams, tests, and procedures are involved in this study?	Please delete the following language from the Informed Consent: **What exams, tests, and procedures are involved in this study?** You and your family may want to know about any genetic test findings that may be important to your health. You may use this form to grant us permission in advance to give this information to your doctor. If a genetic test result about you seems to be medically important and you have granted us permission to contact you, the following steps will occur: 1. Researchers will study the result further to decide if it may be medically important to you or your relatives. 2. The research laboratory that performed the genetic test will contact your doctor about the finding. The research laboratory, which will not have any identifying information about you, will provide your doctor with a code number assigned to your genetic test sample.

#	Section	Comments
		3. Your doctor will use the code number to identify you, and will then contact you about the medically important finding. Your doctor may try to contact you several times. 4. You will require another genetic test to confirm the results. This test must be paid for at your own expense. 5. If it is confirmed that there are changes found that could cause health problems, then your doctor will discuss your options with you. We strongly suggest that you also talk to a genetic counselor. Genetic counseling services must be paid for at your own expense. It is more likely, however, that you will not be contacted by us about a medically important finding. Even if we do not contact you, it does not mean that your genes do not contain changes that are important to your health. Researchers are always learning about new and medically important changes in genes and some information may be learned in the future. Researchers will only decide to contact you about genetic test results at the time your DNA is initially sequenced. You will not be contacted or consented for any research done using your samples in the future, and you will not receive any reports or information about any medically important findings learned in the future. Also, sometimes the meaning of genetic test results can be uncertain, and we may not know for sure what the results mean for your future health. Sharing an uncertain genetic test result with you could offer little benefit, no benefit at all, or could even be harmful. Results from genetic testing will not be a part of your medical records, unless the results are confirmed by additional testing that you agreed to. See "Who will see my medical information?" for laws and risks in protecting your genetic information. *Response: This has been completed*

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of an anti-cancer drug, triapine, to the usual radiation-based treatment (Lutetium Lu 177 Dotatate) for neuroendocrine tumors

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10388, "A phase I trial of triapine and Lutetium Lu 177 Dotatate in combination for well-differentiated somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs)" (NCT # 04234568)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have neuroendocrine tumors, and your cancer is positive for somatostatin receptors.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

What is the highest dose of triapine in combination with Lutetium Lu 177 Dotatate that is safe and tolerable in patients with neuroendocrine tumors?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your neuroendocrine tumor. The usual approach is defined as care most people get for neuroendocrine tumors. There is evidence that the study drug, triapine, can make cancer more sensitive to the usual treatment, Lutetium Lu 177 Dotatate. The combination of triapine and Lutetium Lu 177 Dotatate is not approved by the Food and Drug Administration (FDA) for any cancer.

This is the first time these drugs will be tested together in humans.

What is the usual approach to my neuroendocrine tumor?

The usual approach for patients who are not in a study is treatment with Lutetium Lu 177 Dotatate or everolimus, which are both approved by the Food and Drug Administration (FDA). Everolimus is able to keep the disease stable in 50 out of 100 treated patients for about 11 months. Lutetium Lu 177 Dotatate is able to keep the disease stable in 50 out of 100 treated patients for about 30-35 months.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get triapine, in combination with Lutetium Lu 177 Dotatate for up to 32 weeks.

Your doctor will continue to follow your condition every 3 months from the time of enrollment for 2 years or until your disease gets worse, and watch you for side effects with a procedure that uses a computer linked to an x-ray machine that takes detailed pictures of the areas inside your body. This is known as computer tomography (CT) scan. You will need to come to the clinic every 3 months during this follow up period. This means you will keep seeing your doctor for up to 2 years from the time your enroll in the study. If you stop taking part in the study because you experience an unacceptable adverse event you will be followed until resolution or stabilization of the adverse event.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

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 at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer. Some

risks may be serious and may even lead to death. Combining the study drugs can result in greater similar side effects of those currently experienced by each drug individually.

Some of the most common side effects that the study doctors know about are:

- Anemia (a condition in which the blood cell count is low) which may cause tiredness or may require blood transfusions
- Nausea, vomiting
- Tiredness
- Fever
- Bruising, bleeding
- Infection, especially when white blood cell count is low

There may be some risks that the study doctors do not yet know about.

Benefits

There is some evidence from laboratory-based experiments that adding triapine to the usual approach can kill cancer cells which might result in controlling cancer for longer than the usual approach alone. However, we do not know if this will happen in people. It is unlikely that adding triapine to the usual approach will help you live longer than the usual approach alone. This study may help the study doctors learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the, Institutional Review Board (IRB), FDA, or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the safety of a drug called triapine when used in combination with Lutetium Lu 177 Dotatate. Triapine has been tested in humans, but has not been tested in people with neuroendocrine tumor in combination with Lutetium Lu 177 Dotatate. This study tests different doses of the drug, triapine, to see which dose is safer and more tolerable for people. Another purpose of the study is to check the level of the study drugs in your blood (pharmacokinetics). In addition, another objective of the study is genetic testing using your tumor tissue and blood to see if the combination of drugs may work in treating your type of cancer. There will be about 29 people taking part in this study.

What are the study groups?

There are two parts in this study, a dose escalation part and a dose expansion part. Your doctor will tell you which part you are in.

In the dose escalation part of this study, different people will get different doses of the study drug triapine.

The first 3 people taking part in this study will get the starting dose of triapine. If the drug does not cause serious side effects, the next group of people in the study will get a higher dose. The study doctors will watch each group carefully as they increase the dose. The doses will continue to increase for every new group until people have serious side effects that require the dose to be lower. Once this dose is found, the dose escalation is stopped.

In the dose expansion part of this study, the highest dose with manageable side effects will be given to 14 more people. This will help study doctors better understand the side effects that may happen with triapine.

Treatment schedule: You will get Lutetium Lu 177 Dotatate through a vein in your arm on the first day of each cycle. This will take approximately 30-40 minutes. You will take triapine by mouth either every day or every other day on Days 1-14 of each cycle. Your study doctor will tell you what dose to take. You will be asked to fast (except for water) for 2 hours prior to dosing and for 1 hour after ingesting the oral dose of triapine. Triapine capsules should not be crushed or opened. You should only take triapine for the first 14 days of each cycle and not take triapine until the bottle is empty. Triapine should be stored at room temperature. Each cycle lasts 8 weeks. This study has 4 cycles. See the study calendar for more information.

You will not be able to get additional doses of the drug, triapine. Triapine is not approved by the FDA for treatment of your disease.

What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- A computed tomography (CT) or magnetic resonance imaging (MRI) scan before you begin treatment, every 8 weeks during treatment, and when your disease gets worse.
- A gallium-68 (or Copper-64) positron emission tomography (PET)/CT scan before you begin treatment.
- Blood counts done every 2-4 weeks.
- Physical exams done monthly.
- For women able to have children, a pregnancy test before treatment begins. Short- and long-term safety data on fetuses exposed to 177 lutetium dotatate are currently unknown. Pregnancy testing is being done to exclude pregnant patients from participating in this study.

This study will use genetic tests that may identify changes in the genes in your DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer. Samples for genetic testing will be collected to see if the combination of drugs may work in treating your type of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If the changes in your genes were inherited, the changes could also affect the health of your family members.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

Your study doctor will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer as long as it has been within the past 6 months. This sample is a required part of the study. You and your study doctor will not get the results of this testing.

If there is not enough tissue left over from your biopsy or if was done more than 6 months ago, your study doctor will need to do another biopsy to get this tissue before you begin study treatment. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. This sample will be used to understand the makeup of your tumor. Some genetic changes in the tumor can help us understand why some patients respond to treatment and can lead us to develop new treatments in future. You will not get the results of this testing.

Blood samples will also be taken for the study. The first required blood sample will be collected on the first day of Cycle 1. The second required blood samples will be collected on the first day of Cycle 2. The final required blood samples will be collected when your disease gets

worse. Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA. If you are in the dose escalation group, additional required blood samples will be collected on Day 9 of Cycle 1 (9 times total over 8 hours). These blood samples will help the researchers check the level of the study drugs triapine in your blood at various time points (pharmacokinetics) and if the protein in your red blood cells can carry oxygen. You will not get any results of these blood tests.

A patient study calendar is attached at the end of this document. It shows how often these procedures will be done.

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

General Risks

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 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 study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 7 months after you have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue for a genetic change or changes, for example changes in MEN-1genes. Changes in MEN-1 or multiple endocrine neoplasia gene can increase the chances of development of certain tumors like neuroendocrine tumors and thyroid tumors. These changes can sometime be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection, significant bleeding, or collapsing of the lung can occur. You may sign a separate consent form for the study biopsy that describe the risks in more detail.

Side Effect Risks

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 let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. 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.

This study is looking at a combination of the usual approach used to treat this type of cancer plus a study drug. This different combination of treatment may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and 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.

Possible Side Effects of Triapine
(Table Version Date: March 19, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving triapine more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Nausea, vomiting • Tiredness, fever • Bruising, bleeding • Infection, especially when white blood cell count is low

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving triapine, from 4 to 20 may have:
• Skin changes • Pain • Constipation, diarrhea, heartburn • Sores in the mouth which may cause difficulty swallowing • Chills • Swelling and redness at the site of the medication injection • Change in the heart rhythm • Weight loss, loss of appetite • Dehydration • Dizziness, headache • Changes in taste • Cough, shortness of breath • Hair loss, rash • Flushing • High blood pressure which may cause headaches, dizziness, blurred vision • Low blood pressure which may cause feeling faint

RARE, AND SERIOUS In 100 people receiving triapine, 3 or fewer may have:
• Heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Damage to the lungs which may cause shortness of breath

Possible Side Effects of Lutetium Lu 177 Dotatate

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Lutetium Lu 177 dotatate, from 4 to 20 may have:
• Collection of immediate effects caused by a high dose of radiation, which includes loss of appetite • Bruising, bleeding • Infection, especially when white blood cell count is low
RARE, AND SERIOUS In 100 people receiving Lutetium Lu 177 dotatate, 3 or fewer may have:
• Nausea, vomiting • Cancer of bone marrow caused by chemotherapy • Damage to the bone marrow (irreversible), which may cause infection, bleeding, and may require transfusions

Additional Drug Risks

The study drug could interact with other drugs. Your study doctor will give you a clinical trial wallet card that lists the study treatment. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

Imaging Risks

The gallium 68 (or Copper-64) dotatate scan that you get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The gallium 68 (or Copper-64) dotatate scan that you get in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from this scan is the same as 5 years of exposure to the US national average natural background levels of radiation exposure. This amount of extra radiation has not been found harmful based on current data.

Other Risks and Precautions

Lutetium Lu 177 Dotatate, a beta- and gamma particle-emitting pharmaceutical, is a radioactive therapeutic agent. Though the external radiation exposure associated with Lutetium Lu 177 Dotatate is low, care must be used to keep body fluids from coming in contact with family members or caregivers. Your doctor will give you information on the good hygiene practices to follow to

minimize radiation exposure from bodily fluids to household members and caregivers. Some of the precautions include using disposable gloves when wiping up blood, urine, stools, or vomit, or when handling stained clothes. Clothing soiled with Lutetium Lu 177 Dotatate or patient fecal matter or urine should be washed promptly and separately from other clothing. Use the same toilet each time you use the bathroom in your home, and if possible, use a different toilet than other members of your household. Sit down on the toilet to urinate to keep urine from splashing or spraying. Please follow these guidelines for at least 30 days after each Lutetium Lu 177 Dotatate treatment. Flush the toilet a few times after each use. Contact your health care team with questions you may have related to radiation exposure with Lutetium Lu 177 Dotatate.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- You also will keep a pill diary. This helps you keep track of when you take your pills. The study doctor will show you how to use this diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle.

For women: Do not get pregnant or breastfeed while taking part in this study.
For men: Do not father a baby while taking part in this study.
For all: Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 7 months after your last dose of study drug Lutetium Lu 177 Dotatate.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting Lutetium Lu 177 Dotatate ready and giving it to you.
- your insurance co-pays and deductibles.
- the gallium 68 (or Copper-64) dotatate scan.
- the CT or MRI scans before you begin treatment, every 8 weeks during treatment, and when your disease gets worse.
- 24hr Urine Tests.
- EKG.
- CT Scan.
- For women able to have children, a pregnancy test before you begin treatment.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The biopsy for testing your genetic material at the beginning of the study if archival tissue is not available.
- Research blood draws on the first day of Cycle 1 and when your disease gets worse. If you are in the dose escalation study, the additional research blood draws on Day 9 of Cycle 1. If you are in the dose expansion study, the additional research blood draw on Day 1 of Cycle 1 and cycle 2 and when your disease progresses (worsens).

You or your insurance provider will not have to pay for triapine while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study or the study agent now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The Imaging and Radiation Oncology Core (IROC).

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases,

employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with your cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or

straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect your blood for research on evaluating the changes in your DNA and RNA that occur during treatment. Researchers will obtain genetic material (DNA and RNA) from both your tumor cells and your blood. Your DNA and RNA will be used for genomic sequencing, which is sequencing of all or part of your DNA. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems. The genomic sequencing will be done by an NCI-supported laboratory in Frederick, Maryland, known as the National Clinical Laboratory Network (NCLN) Genomics Laboratory at the Frederick National Laboratory for Cancer Research. The laboratory will compare the genomic sequences from your tumor and blood cells to identify how they differ. The differences between genomic sequences of your tumor and blood cells may be important to understand why you did or did not respond to the treatment you received. Researchers hope to find potential "biomarkers" (changes present in tumor tissue that predict how patients with your type of cancer may respond to current or future treatments). This optional study may improve the ability to select future treatments or treatment combinations for others in the future. This optional study will not affect the cancer treatment or approach that you receive.

Neither you nor your study doctor will be informed when the genetic sequencing research will be done. You and your study doctor will not receive reports of these studies, as they are intended for research purposes only and cannot be used to plan treatment.

Unknown future studies

If you choose to take part in this optional study, any of your tumor tissue or blood samples left over from the genomic sequencing will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Nationwide Children's Hospital in Columbus, Ohio, and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. Your genomic sequence will also be stored in a secure NIH database for future use.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your tumor tissue and blood samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include genomic sequencing.
- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. About 4 teaspoons of blood will be collected from a vein in your arm before you begin study treatment and when your disease gets worse. A sample from the biopsy tissue that is required for this study will also be sent to the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance for exams, tests, and procedures done for research purposes only; these include the blood draws, DNA/RNA sequencing, and biobanking of your specimen(s). You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*),, who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I need my tissue or blood samples to be returned?

Tumor tissue or blood samples that remain in the biobank can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be returned if tissue is needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Tumor tissue or blood samples and genetic material (DNA and RNA) that is no longer in the biobank or that has already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

What if I have questions about this optional sample collection?
If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor[s]*) at (*insert telephone number).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory studies described above.

YES NO

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from these studies.

YES NO

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

This is the end of the section about optional studies.

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 and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature _____

Date of signature _____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature _____

Patient Study Calendar for Protocol 10388

Cycle length = 8 weeks	Screening	Before you begin study treatment	Cycle 1 (8 weeks)							Cycle 2 (8 weeks)				Cycle 3 (8 weeks)				Cycle 4 (8 weeks)				When your disease gets worse	To be conducted at each 3-month follow-up visit for 2 years from enrollment and at off-study evaluation
			Day 1	Day 9	Day 14	Day 15	Day 29	Day 43	Days 44-56	Day 1	Day 14	Day 29	Days 30-56	Day 1	Day 14	Day 29	Days 30-56	Day 1	Day 14	Day 29	Days 30-56		
Triapine			A----------A							A-------A				A--------A				A-------A					
Lutetium Lu 177 dotatate			B							B				B				B					
Pre-study procedures including informed consent, demographics, medical history, and height	X																						
Concurrent meds	X		X----------X																				
Physical exam, vital signs, weight, and an assessment of how well you perform every-day tasks and activities	X		X				X			X		X		X		X		X		X			X
Blood draws for complete blood count and general health status	X		X			X	X	X		X		X		X		X		X		X			X
EKG (as your doctor indicates is necessary)	X																						
Gallium 68 (or Copper-64) dotatate scan	X																						
Side effects evaluation			X----------X																				

Cycle length = 8 weeks	Screening	Before you begin study treatment	Cycle 1 (8 weeks)							Cycle 2 (8 weeks)				Cycle 3 (8 weeks)				Cycle 4 (8 weeks)				When your disease gets worse	To be conducted at each 3-month follow-up visit for 2 years from enrollment and at off-study evaluation
			Day 1	Day 9	Day 14	Day 15	Day 29	Day 43	Days 44-56	Day 1	Day 14	Day 29	Days 30-56	Day 1	Day 14	Day 29	Days 30-56	Day 1	Day 14	Day 29	Days 30-56		
Medical imaging scans for tumor measurements (CT/MRI)	X		Scans should be performed every 8 – 12 weeks.																				X
Pregnancy test	X																						
24-hour Urine test			X																		X		X	
Blood collection for research purposes (Mandatory)			X							X													X	
Blood collection for research purposes (Optional)			X																				X	
Tumor tissue collection for research purposes (Mandatory)[C]		X																						
Blood collection for research purposes to check the level of study drugs in your blood (Dose-escalation group only)				X[D]																				
Blood collection for research purposes to check if the protein in your red blood cells can carry oxygen (Dose-escalation group only)			X	X[D]																				

Cycle length = 8 weeks	Screening	Before you begin study treatment	Cycle 1 (8 weeks)							Cycle 2 (8 weeks)				Cycle 3 (8 weeks)				Cycle 4 (8 weeks)				When your disease gets worse	To be conducted at each 3-month follow-up visit for 2 years from enrollment and at off-study evaluation
			Day 1	Day 9	Day 14	Day 15	Day 29	Day 43	Days 44-56	Day 1	Day 14	Day 29	Days 30-56	Day 1	Day 14	Day 29	Days 30-56	Day 1	Day 14	Day 29	Days 30-56		

A: Triapine: Dose as assigned; given daily on Days 1-14 of each cycle.
B: Lutetium Lu 177 Dotatate: Dose as assigned; given through a vein in your arm on Day 1 of each cycle.
C: If a tumor sample is not available within 6 months of your previous surgery, then you will need a biopsy.
D: Blood collection will happen at various time points