PRINCIPAL INVESTIGATOR: Mark Roschewski, M.D.

STUDY TITLE: A Phase 1 Study of Romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide (RAdR) for relapsed/refractory T-cell malignancies

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: 09/26/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

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). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have an included adult T-cell malignancy (TCM) that has not responded to standard treatments.

The purpose of this study is to test whether the combination of romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide (RAdR) can be used safely in people with your disease. Each of these drugs is approved by the Food and Drug Administration (FDA) for the treatment of other cancers and/ or diseases. The combination of these drugs has not been used before to treat TCM and is not approved by the FDA. We will look at if they are effective in treating your disease. The goals of this study are to determine the safe dose of lenalidomide when combined romidepsin, CC-486 (5-azacitidine) and dexamethasone to be used, to identify the side effects of the combination treatment and its effects on your immune system, and to determine if this treatment has activity against your cancer.

The combination of romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to treat TCM. Since these drugs have never before been given together, this treatment is considered investigational, or experimental. The FDA has given us permission to use romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide together in this study

There are other drugs and treatments that may be used for your disease, and these can be prescribed by your regular cancer doctor, if you are not in this study. These drugs all work in

different ways in the body as compared to romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide, and with different side effects. People with TCM are usually given CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone)-like regimens that produces long-term progression free survival in about 30% of people. If you would prefer other drugs or treatments, you should consider not joining this study.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- In the first groups of participants enrolled (dose escalation), we wanted to find out the highest dose of lenalidomide that is safe to use with romidepsin, CC-486 (5-azacitidine) and dexamethasone. We tested increasing doses of lenalidomide in small groups. We also wanted to find out what kind of side effects these medications might cause. Now that the dose escalation portion is completed, we will enroll additional participants to a second portion of the study (dose expansion) to learn more about whether these study medications can shrink your tumor(s).
- Before you begin the study, we will perform tests to find out whether you are eligible to participate (screening) that will include tests such as: a complete physical examination, blood and urine tests, bone marrow testing and imaging. These tests will be done on a separate screening protocol before signing the informed consent document for this study.
- If you are eligible to receive treatment, during the study, drugs will be given as follows for up to six cycles of 28 days each. You will take lenalidomide on Days 1 to Day 10 for each cycle. This medication is given by mouth. On Days 1 and 10 of each cycle, you will come to the clinic to receive romidepsin by IV infusion and dexamethasone by mouth. CC-486 (5-azacitidine) will be taken by mouth on Days 1-10 of each cycle.
- You may experience side effects from taking part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. Examples of some of the side effects that you may have include: changes in blood counts (such as low red or white cells), gastrointestinal (such diarrhea, nausea, vomiting), rashes, fatigue, and infections. Since this is the first time that romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide are administered together, there may be side effects that we cannot predict.
- You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and to see if the treatment is having any effect on your disease. We will also collect required samples from you (including blood, bone marrow, and tumor biopsies) for both clinical and research purposes. We may also collect saliva or cheek swabs for research.
- After the study treatment has ended, we will need to see you at the NIH Clinical Center periodically for up to about 4 1/2 years to assess your health and to determine what impact, if any, the study drugs may have had on your disease and then annually as your doctor feels is appropriate.

- Because of the possibility of potential harm to an unborn child, if you are a woman capable of becoming pregnant or the man of a partner who may become pregnant you MUST use birth control at least 28 days before starting treatment, throughout therapy (including interruptions in therapy), and for at least 6 months after discontinuation of therapy.

Just as we do not know what side effects you might have, we cannot know if you may benefit from taking part in this study. Even if you do not benefit, this study and the results from our research will help others in the future.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. 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.

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

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?

The purpose of this research study is to test whether the combination of romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide can be used safely in people with your disease.

We are asking you to join this research study because you have an included refractory mature T-cell malignancy (TCM) that has not responded to standard treatments.

Romidepsin interferes with the cancer cell's ability to multiply and leads to cell death. Romidepsin is approved to treat cutaneous T-cell lymphoma (CTCL) or peripheral T-cell lymphoma (PTCL) in people who have received at least one prior systemic treatment.

CC-486 (oral 5-azacitidine) causes the death of rapidly dividing cells, including cancer cells. It is approved by the FDA as maintenance treatment of acute myeloid leukemia in adults who are unable to complete intensive curative therapy, such as stem cell transplantation.

Lenalidomide works to stop the growth of cancer cells by inhibiting the growth of new blood vessels that supply the tumors, block the growth of new cancer cells, and stimulating certain immune cells to attack cancer cells. Lenalidomide is approved for certain anemias and in follicular

lymphoma in people who have already received treatment. It is also approved in combination with dexamethasone for multiple myeloma and in mantle cell lymphomas that have not responded to two prior therapies and is used with rituximab in people with marginal zone lymphomas who have already received treatment.

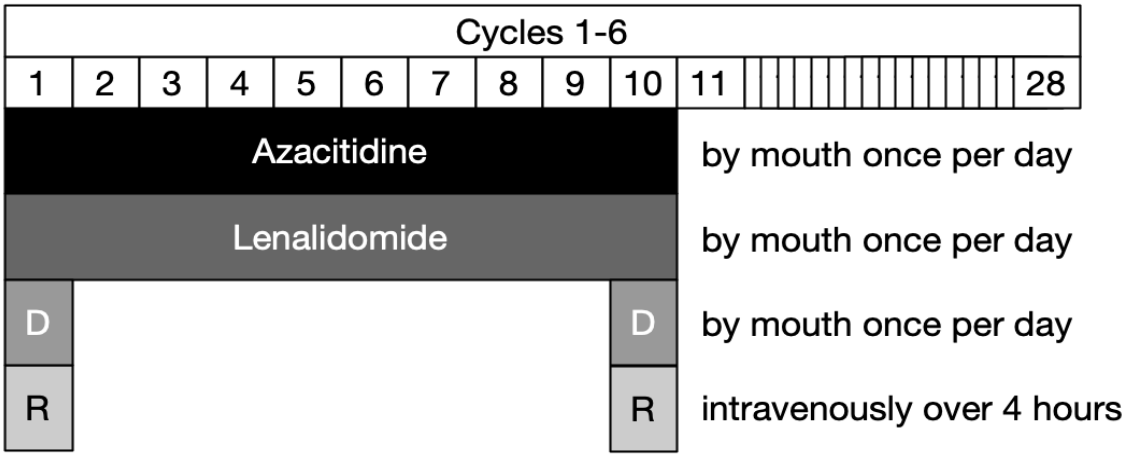
The combination of these drugs is not approved and is considered experimental in this study.

WHAT WILL HAPPEN DURING THE STUDY?

If you decide to take part in this study and you are found eligible to take part, you will be asked to:

- Take lenalidomide by mouth on days 1-10. Romidepsin will be given by IV infusion (by a tube in one of your veins) over 4 hours with oral dexamethasone in the clinic on Days 1 and 10 of each cycle. CC-486 (5-azacitidine) will be taken by mouth on Days 1-10 of each cycle. Each cycle is 28 days and you may remain in study up for up to six (6) cycles.
- The oral medications for this study, lenalidomide and CC-486 (5-azacitidine), can be taken with or without food, swallowed whole, not chewed and should be taken at about the same time every day. Take lenalidomide and CC-486 (5-azacitidine) once a day about 24 hours apart on the days you are supposed to (as stated above).
- You will be asked to keep a diary to record each dose of the oral medications, lenalidomide and CC-486 (5-azacitidine), that you take outside of the clinic for this study. We will be reviewing this diary with you during your visits to the clinic, so please bring it to every visit. Additionally, a member of the team will discuss with you any issues that might be barriers to taking your medications.
- At each clinic visit at the NIH Clinical Center, please bring your completed medication diary pages and all of your tablet containers (whether they are empty or not) as we will be counting the tablets and reviewing your diary pages.
- In order to confirm that the doses are safe, participants will be enrolled in groups:
    - Dose escalation-in groups: First, a group of 3 - 6 study participants received 5mg of lenalidomide. When there were no safety issues, the next group of participants received 10mg of lenalidomide. When that dose proved to be safe, the next group of participants received 15mg of lenalidomide. When there were no safety issues at that dose, the final group of participants received 20 mg. Each group was checked closely for side effects for at least 4 weeks before enrolling the next higher dose level of lenalidomide.
    - Dose expansion: Now that the recommended dose of lenalidomide with romidepsin, CC-486 (5-azacitidine) and dexamethasone has been established, up to 9 participants will be treated with the drugs and their effectiveness in the treatment of TCM.
- Participants in the dose expansion group will be given treatment on an outpatient basis unless decided otherwise by the physician, based on clinical judgment.

Another way to find out what will happen to you during the study is to read the chart below. Each number is one day. Start reading at the left side and read across to the right:



Key: D=dexamethasone and R=Romidepsin

Before you begin the study

Before you begin the study, you will have several tests performed to check whether the study is suitable for you. These tests will be done on another study before you can sign the informed consent document for this study. This is called screening. Your doctor will review your medical history and the drugs that you are currently taking as well as the previous treatments of your disease to determine whether you can participate in this study.

A previously collected blood sample or small part of your tumor tissue (depending on your disease) that was collected from any previous surgery or biopsy will be tested at NCI to confirm your diagnosis. If no sample is available or if additional sample is needed to confirm your diagnosis, a fresh blood sample or biopsy will be taken. A biopsy will also be done prior to treatment if there is not enough tissue available from your diagnostic biopsy for study purposes. Any leftover tissue may be stored for future research studies, but a biopsy will not be performed solely for these studies. You will be told if this biopsy is needed.

If you have had some of these tests or procedures recently, they may or may not have to be repeated.

During the study

If the screening process shows that you are eligible for the study, and you choose to be in it, you may need to have a few additional standard tests completed if not done recently. You will also have additional samples collected for research tests.

You will come to the NIH Clinical Center for treatment and procedures. The treatment will be given in the outpatient setting at the Clinical Center for most of the study unless decided otherwise by the study team based on clinical judgment. You will be given romidepsin as described in section "What will happen during the study?," over a 4-hour period. Your dose of lenalidomide will be assigned depending on what dose level is open at the time of your enrollment during dose escalation or at the maximum tolerated dose during the dose expansion portion.

Participants who are not already on blood thinners will be given oral aspirin 81mg to take for prevention of blood clots when starting lenalidomide. We will give you a medication by mouth or by IV to help with nausea when getting romidepsin and CC-486 (5-azacitdine) for the first cycle. This may be omitted in subsequent cycles if your doctor feels it is not necessary. Additional medications may also be given as standard of care if disease is detected in your brain or spinal cord. Your study doctor or a member of the study staff can explain these to you in more detail. Because of the unknown side effects, we will ask you to stay at the clinic for an additional 30 minutes after your infusion so we may monitor you.

Certain medications and/or live vaccines, need to be used with caution or avoided all together while you are participating on this study. If any physician other than the study team prescribes a medication or vaccine for you for another condition, or you take any new over-the-counter medications, vitamins or herbal supplements, you must tell us and check with us prior to starting. This is important because the interaction of some medications may cause serious side effects and/or may still be unknown. You should also avoid grapefruit products and Seville oranges as these may affect how your body processes the study medications. You study team will discuss what medications to avoid during your study participation.

You must NEVER donate blood while you are participating in this study and for at least 28 days after you have been discontinued from the study.

Similar to the tests done at the beginning of the study, the following will be repeated during the study to see how you are doing and how the cancer may be responding to treatment:

- Review of medical history, and a physical exam (check weight and vitals), including obtaining information about how you function in your daily activities, side effects and symptoms, and review of medications
- Routine blood and urine tests
- For women who can have children, a pregnancy test will be done within 10-14 days and again at 24 hours before starting treatment. You will not be able to participate if you are pregnant or you are breast feeding because we don't know how this medicine would affect your baby or your unborn child. Women with regular or no menstrual cycles will have pregnancy tests weekly for the first 28 days of lenalidomide treatment, including dose interruptions and then every 28 days throughout the remaining duration of lenalidomide treatment, including dose interruptions, at lenalidomide discontinuation, and at Day 28 following lenalidomide discontinuation. If menstrual cycles are irregular, the pregnancy tests will be done weekly for the first 28 days of lenalidomide treatment, including dose interruptions, and then every 14 days throughout the remaining duration of lenalidomide treatment, including dose interruptions, at lenalidomide discontinuation, and at Day 14 and Day 28 following lenalidomide discontinuation.
- Bone marrow testing and imaging:
    - Bone marrow testing will be repeated at the end of study treatment if needed to confirm response, if and only if other tests show a complete response.

- Participants with skin involvement, as determined by the study doctor, will have a skin assessment to evaluate their skin disease.
- Tumor imaging (such as, CT scan, PET/CT) will be done to assess the sites of your disease every 6 weeks during treatment. An MRI of the brain and lumbar puncture is only required in participants with neurological symptoms. In participants with disease primarily on their skin, clinical photography and evaluation by a dermatologist will be used to assess the disease sites present on the skin. Other body areas may be imaged if clinically indicated. If your disease does not progress, follow-up imaging may be done every 60 days for the first 6 months after treatment, then every 90 days for 2 years and then every six months for another 2 years and then annually until you start another treatment, your disease progresses or the study ends.

Standard of Care Treatment

You may be asked to sign a separate consent form for any standard of care procedures not outlined in this consent.

Additional research testing

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study therapy, we will also collect samples from you for purposes of research only. The samples are being done to look at the effects of therapy on your immune system and markers of tumor activity, including collecting and testing tumor cells. Unless noted otherwise below, the samples will be collected at least once each cycle and at the time your disease responds to treatment or gets worse (required), and at the end of treatment (optional).

The samples included for these studies include:

- Blood Samples: Blood samples will be collected for required research studies to learn more about how the study drugs affect your body, the cancer, and your immune system, and to check for levels of some of the study drugs in the body. Collection of blood will be drawn before treatment, three times during Cycle 1, two times during subsequent cycles, and at follow-up visits.
- Cheek Swab or Saliva Samples: A required cheek swab and/or saliva sample to collect normal tissue will be done, likely at the beginning of the study only. To obtain a cheek swab, a small brush is rubbed against the inside of the cheek to wipe off some cells. To obtain saliva, a special collection tube will be used, and it may take a few minutes to collect the saliva.
- Tumor Tissue and Biopsies: A portion of the biopsies done in the past for your cancer will be collected and are required. We will ask you to undergo an optional tumor biopsy for research at the start if Cycle 1 and on Day 15 of Cycle 1 and if your disease should progress during or after treatment, only if it is safe to do so. The biopsies are being collected for special research tests. You will be given an opportunity to decide at the time of each procedure. You may agree to biopsies now and change your mind later. If at any time you do not want to have a biopsy done, please tell us.

Usually tissue can be obtained safely and comfortably with local anesthesia; however, you may receive conscious sedation before undergoing a biopsy. Conscious sedation is usually given to help someone relax and minimize discomfort. It can be given as a pill, a shot, an IV or even inhaled. You may have to wait up to an hour to start feel the effects depending on how it is given. Once it takes effect, you will be mostly awake, though relaxed or drowsy. You will be monitored throughout the procedure. Biopsies will NOT be done on this study if they require general anesthesia. We may ask that you have ultrasound to help clearly locate your tumor when doing a biopsy.

All of your samples collected for research purposes on this study may be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) in the cells carries genetic information and passes it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow.

To look at your DNA, we may do what is called "whole genome sequencing." This where we will do special tests in the lab to look at the entire sequence, or order, of how your DNA is put together. This is what makes you unique.

To determine which parts of the DNA have mutated, we will compare the DNA in your tumor cells to DNA from your normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There may be exceptions to what we share with you and this is described later in this consent form in the section for "Return of research results."

When you are finished taking the drugs (treatment)

When you finish taking the experimental therapy, we will ask you to come to the clinic for follow-up visits and assessments at about the following times after treatment: 30 days after stopping treatment for a safety visit, every 60 days for the first 6 months, then every 90 days for 2 years and then every six months for another 2 years. After 4 ½ years, we want to see you annually to monitor your disease status. These clinic visits will include having required physical exam, skin assessment, MRI/lumbar puncture, blood samples collected for routine analysis and for research, and may include CT or PET/CT scans. Visits usually take about 3 hours but should take no longer than 8 hours.

If your disease worsens, or you start need to start a new anti-cancer we will continue to follow-up with you by phone every 3-6 months to see how you are doing, until we complete the main research goals of the study, which we expect will take 4-5 years.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for at least 4 ½ years.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 30 people participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE 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.

Risks of Romidepsin

You may have side effects from the romidepsin while on the study. Romidepsin may cause serious side effects that can be severe or life-threatening infections, including pneumonia, sepsis, and viral reactivation including Epstein Barr and hepatitis B virus.

Please talk to us about any symptoms you have while you are in the study.

In studies with humans, common and not very common risks and side effects related to the romidepsin included the following:

Very Common >10% In 100 people receiving romidepsin, more than 10 may have:
• Anemia (low red blood cells) • Low number of white blood cells, cells that help fight infection (leukopenia, neutropenia, granulocytopenia, lymphopenia) • Low platelets, cells that help blood to clot (thrombocytopenia) • Abnormal heart rhythm (tachycardia) • Abdominal pain, constipation, diarrhea, nausea, vomiting • Tiredness, fever, chills • Swelling • Skin infections, dry, itchy, red and/ or swollen skin • EKG changes • Weight loss, loss of appetite • Headache • Changes in taste, swelling and/ or sores in mouth • Cough, Shortness of breath • Low blood pressure • Increases in blood levels of liver function tests • Increases in blood levels of bilirubin, creatinine, glucose, magnesium, uric acid • Decreases in blood levels of albumin, calcium, potassium, magnesium, sodium, phosphorus

Common ≥1% and <10% In 100 people receiving romidepsin, 1 to 10 may have:
• Low number of white blood cells, cells that help fight infection, with a fever (febrile neutropenia) • Chest pain • Injection site reaction (redness, pain, itching or swelling near site of infusion)

Common ≥1% and <10% In 100 people receiving romidepsin, 1 to 10 may have:
• Heartburn, swelling and/ or sores in mouth • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Cellulitis (skin infection – skin may be swollen red, painful, warm) • Shingles • Oral candidiasis/ thrush (may have white lesions in mouth, redness, burning, soreness in mouth) • Lung problems (Pneumonia, pleural effusion, upper respiratory infection) - symptoms may include new or worsening cough, chest pain, shortness of breath. • Urinary tract infection - symptoms may include burning sensation with urination, urge to urinate, cloudy urine, pain • QT prolongation on EKG • Abnormal heart rhythm (supraventricular arrhythmia) • Tumor lysis syndrome – symptoms may include irritability, weakness, nausea, vomiting, diarrhea, muscle cramping, joint pain • Dehydration • Fainting • Low blood oxygen – symptoms may include changes in skin color, confusion, cough, fast heartbeat, shortness of breath • Deep vein thrombosis (a blood clot that forms in a deep vein) – symptoms may include pain, swelling, tenderness, redness • Sepsis – symptoms may include, rapid heartbeat, fever, chills, sweating, confusion, pain, shortness of breath

Uncommon ≥0.1% and < 1% In 100 people receiving romidepsin, up to 1 may have:
• Heart stops working (cardiac failure, congestive heart failure) • Low oxygen to heart tissue (myocardial ischemia) • Multi-Organ Failure • Sepsis caused by a fungal infection that enters the blood and can affect heart, brain, eyes and other parts of the body • Septic shock caused by drop in blood pressure that can lead to respiratory or heart failure, stroke, failure of other organs, and death.

Uncommon ≥0.1% and < 1% In 100 people receiving romidepsin, up to 1 may have:
• Kidney problems, including kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling • Respiratory distress syndrome – Symptoms may include: new or worsening cough, chest pain, shortness of breath, rapid breathing

Risks of CC-486 (5-azacitidine)

You may have side effects from the CC-486 (5-azacitidine) while on the study. CC-486 (5-azacitidine) may cause serious side effects that can be severe or life-threatening: fever, infections, including pneumonia, sepsis, and bleeding of your digestive track or into your brain.

Please talk to us about any symptoms you have while you are in the study.

In studies with humans, common and not very common risks and side effects related to the CC-486 (5-azacitidine) included the following:

Very Common >10% In 100 people receiving CC-486 (5-azacitidine), more than 10 may have:
• Weakness, tiredness • Fever • Pneumonia, shortness of breath • Anemia (low red blood cells) • Low number of white blood cells, cells that help fight infection; with or without fever (leukopenia, neutropenia, febrile neutropenia, granulocytopenia, lymphopenia) • Low platelets, cells that help blood to clot (thrombocytopenia) • Abdominal pain, constipation, diarrhea, nausea, vomiting • Chest pain • Weight loss, decreased appetite • Decreased blood levels of potassium • Muscle and joint pain • Dizziness, headache • Itching, rash, tiny purple, red, or brown spots on the skin

Common >1% and <10% In 100 people receiving CC-486 (5-azacitidine), 1 to 10 may have:
• Low levels of all types of blood cells – white blood cells, red blood cells and platelets (pancytopenia)

Common >1% and <10% In 100 people receiving CC-486 (5-azacitidine), 1 to 10 may have:
• GI bleeding including mouth, hemorrhoids diverticulitis (inflammation in the digestive system – symptoms may include abdominal pain, fever, nausea, and a change in bowel habits.) • Heartburn, swelling and/ or sores in mouth, fungal infection of the mouth • Chills • Cellulitis (skin infection – skin may be swollen red, painful, warm) • Sepsis – symptoms may include, rapid heartbeat, fever, chills, sweating, confusion, pain, shortness of breath • Sinus infection • Sore throat, runny nose, sneezing, stuffiness • Urinary tract infection - symptoms may include burning sensation with urination, urge to urinate, cloudy urine, pain • Dehydration Muscle spasms • Pain – back and bone • Increased blood levels of creatinine • Dizziness, intracranial hemorrhage (bleeding inside the skull) • Lack of energy, drowsiness, trouble sleeping • Kidney failure, blood in urine • Fainting • Lung problems (pleural effusion, respiratory infection) - symptoms may include new or worsening cough, chest pain, shortness of breath. • Hair loss • Skins lesions, hives, redness • Bruising • High blood pressure which may cause headaches, dizziness, blurred vision • Low blood pressure • Nose bleeds

Uncommon >0.1% and < 1% In 100 people receiving CC-486 (5-azacitidine), up to 1 may have:
• Redness of the eye • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Anxiety

Uncommon >0.1% and < 1% In 100 people receiving CC-486 (5-azacitidine), up to 1 may have:
• Fungal pneumonia

Risks of lenalidomide

You may have side effects from the lenalidomide while on the study. lenalidomide may cause serious side effects that can be severe or life-threatening infections, including pneumonitis, serious dermatologic reactions, angioedema and cardiac events.

Please talk to us about any symptoms you have while you are in the study.

In studies with humans, common and not very common risks and side effects related to lenalidomide included the following:

Very Common ≥10% In 100 people receiving lenalidomide, more than 10 may have:
• Anemia (low red blood cells) • Low number of white blood cells, cells that help fight infection; with or without fever (leukopenia, neutropenia, febrile neutropenia, granulocytopenia, lymphopenia) • Low platelets, cells that help blood to clot (thrombocytopenia) • Abdominal pain, diarrhea, nausea, heartburn, vomiting • Tiredness, weakness • Increases in blood levels of liver function tests • Sinus infection • Urinary tract infection - symptoms may include burning sensation with urination, urge to urinate, cloudy urine, pain • Inflammation of the lining of the intestines – signs of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness • Increases in blood levels of glucose which leads to tiredness, frequent urination or excessive thirst • Decreases in blood levels of calcium and potassium • Back, bone and muscle pain, muscle spasms • Tremors • Kidney problems, including kidney failure signs of kidney problems may include decrease in the amount of urine, blood in your urine, ankle swelling • Blood clot which may cause swelling, pain, shortness of breath • Headache • Blurred vision, cloudiness of the eye (cataract), • Swelling (peripheral edema)

Very Common ≥10% In 100 people receiving lenalidomide, more than 10 may have:
• Dry skin, itching, rash • Muscle weakness • Chills, fever • Weight loss, loss of appetite • Feeling of "pins and needles" in arms and legs • Depression, difficulty sleeping • Dizziness • Change in taste

Common >1% and <10% In 100 people receiving lenalidomide, 1 to 10 may have:
• Low levels of all types of blood cells – white blood cells, red blood cells and platelets (pancytopenia) • Abnormal heart rhythm (atrial fibrillation, tachycardia) • Heart stops working (cardiac failure, congestive heart failure) • Low oxygen to heart tissue (myocardial ischemia) • Infection, especially when white blood cell count is low • Dry mouth, toothache • Dehydration • Numbness, tingling or pain of the arms and legs • Change in mood • Lung problems (lung infection respiratory infection, respiratory distress) - symptoms may include new or worsening cough, chest pain, shortness of breath, rapid breathing • Increased sweating • Sores on the skin • High blood pressure which may cause headaches, dizziness, blurred vision • Low blood pressure • Fainting, increased risk of falls • Liver disease which may cause yellowing of eyes and skin, itching, dark urine, abdominal pain • Chest Pain • Herpes simplex and zoster (shingles), including ophthalmic herpes zoster (shingles of the face and eyes) • Cellulitis (skin infection – skin may be swollen red, painful, warm)

Common >1% and <10% In 100 people receiving lenalidomide, 1 to 10 may have:
• Inflammation of the brain (meningitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck • Sepsis – symptoms may include, rapid heartbeat, fever, chills, sweating, confusion, pain, shortness of breath • Bruising • Stroke • A condition with high blood sugar (diabetes) which leads to tiredness, frequent urination or excessive thirst Gout • Increases in blood levels of calcium, uric acid and iron • Decreases in blood levels of phosphorus, magnesium and sodium • Infections of the joint • Tumor lysis syndrome or Tumor Flare Reaction- symptoms may include irritability, weakness, nausea, vomiting, diarrhea, muscle cramping, joint pain

Uncommon ≥0.1% and < 1% In 100 people receiving lenalidomide, up to 1 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Anaphylaxis • Damage to the lungs which may cause shortness of breath • Infection of the appendix • Inflammation of the colon caused by the bacteria, clostridium difficile – signs may include watery diarrhea, fever, loss of appetite, nausea, pain, tiredness • Small intestinal blockage • Bleeding into stomach and intestine (gastrointestinal hemorrhage) • Low blood oxygen (hypoxia)

Other possible treatment side effects:

Rhabdomyolysis and increased bilirubin: One participant on this study experienced rhabdomyolysis, a serious condition in which muscle tissues breakdown. The damaged muscles release proteins and electrolytes that can damage the kidneys and heart and lead to permanent disability or even death. Symptoms of rhabdomyolysis may include: dark and/ or decreased urine, weakness and muscle aches. The participant has recovered and no other participants on this study have had rhabdomyolysis. You will be asked if you have any muscle tenderness and have this assessed by physical exam and if the doctors have any suspicion that you are experiencing this problem, appropriate tests will be performed to determine if you are experiencing this side effect.

- Dexamethasone:
  - Common side effects include: sleep problems (insomnia), mood changes, increased appetite (which may include gradual weight gain), fluid retention, acne, increased sweating, skin changes (including dry skin, thinning skin, bruising or discoloration), slow wound healing, headache, dizziness/spinning sensation, nausea, stomach pain, bloating, and changes in the shape or location of body fat (especially in your arms, legs, face, neck, breasts, and waist), increases in blood levels of liver function tests, menstrual irregularities, increase in blood glucose levels, increase in blood pressure
  - Rare, but serious: anaphylaxis, angioedema, changes in heart rhythms, heart failure, blood clots , changes in vision, eye pain, severe changes in mood (such as depression or extreme happiness), pancreatitis, very low potassium, and very high blood pressure.
  - Some of these side effects are seen with prolonged and continued use of dexamethasone. Please contact the study staff if you are experiencing a side effect or think you might be having a severe reaction.
- Secondary malignancy: Participants with cancer have a higher risk of developing another or second new cancer when compared to people without cancer. These include solid tumors, skin cancer, and cancers of the blood. Participants should make their doctors aware of their medical history and any concerns they may have regarding their own increased risk of other cancers. The study team will be checking you for any possible new cancers that may develop during or following your treatment
- Infection risks: It is important to emphasize that when you have a decreased white blood cell count you are at risk of infection. Such infections can be very serious and can even cause death if not quickly and properly treated. You must call your doctor immediately if you have a temperature greater than 38.3oC (101oF), or if your temperature is higher than 38oC (100.4oF) two times in a 24-hour period.
- Bone marrow failure: Chemotherapy may also cause your platelets to reduce; since platelets are the blood elements that permit blood to clot, this may place you at increased risk of serious bleeding. It may be necessary to give you transfusions of platelets if your platelet counts reach very low levels. There is a small chance that damage to the normal bone marrow may eventually result in bone marrow failure, leading to a serious decrease and shortage of one or more kinds of cells in the blood.
- Tumor Lysis Syndrome (TLS) and Tumor Flare Reaction (TFR): Unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells have happened during treatment of cancer and sometimes even without treatment. This may lead to changes in kidney function, abnormal heartbeat, or seizures. Your study doctor may do blood tests to check for TLS.

Other Study Risks

- Blood draws: The possible side effects of drawing blood include pain, bleeding, bruising, dizziness, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein. Up to about 9

tablespoons of blood may be collected at any day, up to about 26 tablespoons may be collected within 8 weeks.

- Bone marrow biopsy and aspirate: A numbing agent that can cause a stinging or burning sensation may be injected at the site of your bone marrow biopsy. The biopsy needle will go through the skin into the bone and may produce a brief, sharp pain. As the bone marrow liquid is taken from the bone, there may be a brief, sharp pain. Since the inside of the bone cannot be numbed, this procedure may cause some discomfort, however not all people experience discomfort. The possible side effects associated with a bone marrow biopsy include pain, bleeding, bruising, and infection, as well as a reaction to the numbing agent.
- Tumor biopsy: The likely side effects include discomfort or pain, redness, swelling, and/or bruising at the site of the needle insertion. Bleeding from the site of the needle insertion is a less likely risk. Rarely, significant infection or bleeding from this procedure, allergic reaction to the anesthetic, or formation of a scar at the site of needle entry occurs. If you will have sedation with the procedure, the most common risks of conscious sedation last up to a few hours after being given can include drowsiness, feeling slow or sluggish, low blood pressure, headache, and nausea.
- Saliva Capture and/or Buccal Swab collection: There is no risk associated with the saliva capture collection. There are no physical risks with the buccal swab, but you might experience momentary discomfort.
- IV Catheter Insertion: A non-tunneled central catheter is a soft tube a doctor puts into a vein in your arm or in a vein leading to your heart. It is a way to take blood samples or give you fluids, medicines, or nutrients over a long period of time. Possible side effects include pain, bleeding, bruising, and, on rare occasions, swelling in your arm, chest, neck, or face on the same side as your catheter or infection.
- CT, PET and MRI scans: CT, PET, and/ or MRI scans will be used to monitor your disease while you are in this study. CT and PET scans expose you to radiation; the amount depends on the number of body areas scanned. In addition, CT, PET and MRI scans involve use of contrast (oral and/or IV) so that the cancer may be seen better on the images. An IV line may need to be inserted for administration of the contrast agent. This can cause pain at the site where the IV is placed and carries a small risk of bruising or infection. In the small group of people who have a reaction, the most common symptoms are nausea, pain in the vein where the contrast was given, headache, a metallic or bitter taste in the mouth, and a warm or flushing feeling that lasts from 1-3 minutes. Rarely, these symptoms may require treatment. In very rare cases, people have had more severe allergic reactions that result in skin rashes, shortness of breath, wheezing, or lowering of the blood pressure. However, these are considered standard of care to monitor your disease. It is likely that you have had these types of scans already in your diagnosis or treatment. If you have any questions, please ask the study team.

Radiation Exposure from Imaging

During your participation in this research study, you will be exposed to radiation from CT of the neck, chest, abdomen, and pelvis, and from ^{18}F-FDG PET/CT of the torso and the extremities. The

amount of radiation exposure you will receive from these procedures is equal to approximately 14 rem. 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 and ^{18}F-FDG PET/CT that you get in this study will expose you to the roughly the same amount of radiation as 38 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 0.6 out of 100 (0.6%).

MRI RISKS

Your doctor may want you to get a magnetic resonance imaging (MRI) scan. MRI uses a strong magnetic field and radio waves to take pictures of the body. We will obtain pictures of your brain for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. We will place soft padding or a coil around your head. You will be in the scanner about 45 minutes. You may be asked to lie still for up to 15 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at anytime.

It is very important for the experiment that you do not move your head or body inside the scanner. We will use padding around your head to help keep it in place.

We may place a bar in your mouth to help keep your head still.

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 scans:

Procedure

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

Risks

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" which 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 not normal or if you received gadolinium within the previous month.

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.

We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

What are the risks related to pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 28 days after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

The use of lenalidomide in pregnant females and nursing mothers has not been studied nor has the effect of lenalidomide on human eggs and sperm. Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance meaning that it causes severe life-threatening birth defects. The possibility lenalidomide causing severe birth defects cannot be ruled out. Therefore, a plan to prevent pregnancy must be followed.

Men must **NEVER** donate sperm or semen while participating in this study and for at least 3 months after the study drugs are stopped.

All study participants must be registered into the mandatory Revlimid REMS™ program.

You will be required to use **TWO** reliable forms of birth control, one highly effective method and one additional effective method at the same time or practice complete abstinence from heterosexual intercourse for *at least 28 days before starting treatment*, throughout therapy (including interruptions in therapy), and for *at least 3 months after discontinuation of therapy* for men, and for *at least 6 months after discontinuation of therapy* for women.

Effective forms of birth control include:

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

Additional effective method options:

- male latex condom
- diaphragm
- cervical cap

In addition, females of childbearing potential that might be caring for you should not touch the lenalidomide capsules or bottles unless they are wearing gloves.

Privacy Risks Associated with Genetic Testing

It may be possible that genetic information from you could be used by law enforcement agencies or other entities to identify you or your blood relatives

Psychological or Social Risks Associated with Return of Incidental or Secondary Findings

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.

Although 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 research 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.

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.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

The benefit of taking romidepsin, CC-486 (5-azacitidine), dexamethasone, and lenalidomide together is unknown. All of these drugs have shown clinical activity when given to people with T-cell malignancies alone and in combination, and were shown in the lab to block multiple pathways that malignant T cells need to grow and survive. Talk to your doctor about other approved agents and treatments that are available to you and that may provide clinical benefit without taking part in this study.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because of the knowledge gained from the study drug combination or the results of the research studies.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could.

- choose to be treated with surgery, radiation or with drugs already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

When we are examining your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as “incidental medical findings”.

These include:

- 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.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to provide another sample to verify the findings we have seen in our lab. 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).

EARLY WITHDRAWAL FROM THE STUDY

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 worsens or comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if you become pregnant
- if romidepsin, CC-486 (5-azacitidine) or lenalidomide become unavailable
- if new information shows that another treatment would be better for you
- if you do not follow the study rules
- if the study is stopped for any reason

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

After therapy is stopped we would like to see you for a safety visit 30 days after your last dose.

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 Bristol Myers Squibb (BMS) or designated representatives.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will Your Specimens or Data Be Saved for Use in Other Research Studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding mature T-cell malignancies, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will Your Specimens or Data Be Shared for Use in Other Research Studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future

research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

Will Your Genomic Data Be Shared Outside of This Study?

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

How Long Will Your Specimens and Data be Stored by the NIH?

Your specimens and data may be stored by the NIH as long as the study is open. When this study is closed, we may keep the data and any samples that are leftover for future research indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

You will not receive compensation for participation in this study.

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

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

If your travel to the NIH Clinical Center (e.g., flight, hotel) is arranged and paid for by the NIH, the agency making the reservations and their representatives will have access to your identifiable information.

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.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI 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.

Bristol Myers Squibb is providing the romidepsin, CC-486 (5-azacitidine) and lenalidomide for this study to NIH without charge. No NIH employee involved in this study receives any payment or other benefits from Bristol Myers Squibb.

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

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code

to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

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, Center for Cancer Research, or their agent(s)
- Qualified representatives from Bristol Myers Squibb, the pharmaceutical company who produces the romidepsin, CC-486 (5-azacitidine) and lenalidomide.

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

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 information that 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 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, Dr. Mark Roschewski, mark.roschewski@nih.gov, 240-760-6183. 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 should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

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: _____.