PRINCIPAL INVESTIGATOR: Robert Yarchoan, M.D.

STUDY TITLE: A Phase I/II Study of the Safety, Pharmacokinetics and Efficacy of Pomalidomide (CC-4047) in the Treatment of Kaposi Sarcoma in Individuals With or Without HIV

STUDY SITE: NIH Clinical Center

Cohort: *Standard*

Consent Version: *11/29/2021*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need 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 for themselves, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in this study. For the remainder of this document, the term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

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

WHY IS THIS STUDY BEING DONE?

This is a research study to gain information on the use of an anti-cancer medicine called pomalidomide (also called CC-4047) in people with Kaposi sarcoma (KS), whether or not the Kaposi sarcoma is associated with acquired immunodeficiency syndrome (AIDS) or human

immunodeficiency virus (HIV) infection. We would like to obtain information on the side effects and blood levels of pomalidomide in people with KS. In addition, the study will look for any evidence of a beneficial effect of treatment with pomalidomide on the KS lesions or the quality of life of individuals with KS, but this is not the primary purpose of the study. The use of pomalidomide in KS is experimental. Pomalidomide (CC-4047) is a medicine taken by mouth (orally). It belongs to a group of medicines called immunomodulatory drugs (IMiDs) that is in the same family of drugs as thalidomide. The effects of drugs in this class include modifying or regulating the functioning of the immune system, and they also have effects on the body's production of new blood vessels. Pomalidomide is chemically similar to two other medicines, thalidomide and lenalidomide, and both of those medicines have been approved by the Food and Drug Administration (FDA), the USA drug approval agency, for treatment of patients with a blood cancer called multiple myeloma. The effects of pomalidomide on the immune system and on blood vessels may be beneficial in KS, as it acts against some of the factors that are thought to be important in the development and growth of KS. However, this has not been proven. The related drug thalidomide has been used in people with KS, and has been shown to have beneficial effects on the lesions in some subjects. However, thalidomide has not at this time been approved by the Food and Drug Administration for treatment of KS.

Why are you being asked to take part in this study?

You are being asked to take part in this study so that we may evaluate this new medicine in people, like yourself, who have Kaposi sarcoma, whether or not the KS is related to AIDS or HIV infection.

How many people will take part in this study?

We plan to enroll between 25 and 40 subjects in this study.

Description of Research Study

If you consent to participate in this study, you will take pomalidomide tablets each day for three weeks (21 days), followed by a one week (7 day) "rest" from the tablets. Together these three weeks taking medicine and one rest week are called a "cycle" of therapy. Pomalidomide therapy will continue for six cycles (six months) unless your KS completely disappears in less time or you have unacceptable side effects from the pomalidomide. If you still have KS at the end of the six cycles but it seems that your KS is improving, you may be able to continue pomalidomide for up to an additional six cycles. The time period described above is called the initial (or first) course. After you finish the initial course of therapy with pomalidomide, we will continue to follow you for an additional 5 years with infrequent visits and communication with your primary care doctor to monitor for any late side effects or toxicity from pomalidomide and to follow the course of your KS.

If during this time you again develop KS that requires treatment, you may be able to receive a second (optional) course of therapy with pomalidomide. This would be considered if your KS improved with the initial course of therapy and if you and your physician consider that a second (optional) course would be appropriate. If you did receive this second course, it would again be for six cycles (six months) unless the KS disappears in less time or you have unacceptable side effects from the pomalidomide. If in the second course you still have KS at the end of six cycles but it seems that your KS is improving you may be able to continue pomalidomide for up to an additional six cycles.

A detailed description of what will happen if you take part in this study, as well as a list of potential risks and discomforts associated with participation in the study are listed below.

What will happen if you take part in this research study?

Before you begin the study

Before you begin the study, you will be evaluated by a physician investigator, as well as other members of the research team for eligibility to participate in the study. We will discuss your medical history in detail and draw blood from a vein to perform laboratory tests to help determine whether you are eligible to participate. You will also have a chest X-ray to make sure that you are eligible to participate and to document whether KS affects your lungs. We will also need a small sample of tissue (biopsy) from a KS lesion in order to confirm your diagnosis. If you have already had a biopsy, we will work with you to have the biopsy sent to pathologists at the NCI for review. If you have not have not had a biopsy, we will arrange for a biopsy to confirm the diagnosis of KS. If you undergo a biopsy at NIH for diagnostic reasons, we may use a portion of that tissue for research purposes as well. If the reason you are having a biopsy is for your medical care, we will not take additional tissue unless you give us permission to do so. Rather, the amount of the tissue taken will be defined by the medically indicated procedure.

Depending on your symptoms and the results of your chest X-ray and blood tests, we may perform additional tests to determine where in the body you may have KS lesions. These tests could include CT scans or the examination of the lungs or gastrointestinal tract with an endoscope (a flexible instrument to examine the interior of the organ). We will discuss these tests and the reasons they are required if you need to have them. These scans would be done for your clinical care, not for the research.

Before you start pomalidomide, we will also ask that you complete a paper questionnaire asking about the effects of your illness on your day-to-day activities and mood (together called quality of life). You be asked to repeat the same questionnaire once more while you are taking pomalidomide, and again after you stop taking the medicine.

During the study

During the initial course of the study (and the second optional course, if applicable), you will receive pomalidomide at a dose of 5 mg. You will take pomalidomide tablets by mouth every day for the first three weeks of a four week cycle. There is one rest week before starting the next cycle. Pomalidomide should be taken each morning at approximately the same time. You should fast (drink water only) for at least two hours before and at least 30 minutes after taking pomalidomide. You will be asked to complete a medication diary and to return any unused study drug and empty bottles to the clinic at each visit.

All subjects will take either a "baby" aspirin or another medicine to reduce the chance of blood clotting. Those with HIV will also be required to be on combination antiretroviral (anti-HIV) medications. In addition, all subjects taking pomalidomide must follow strict guidelines for prevention of pregnancy. This is because there is a risk of harm to a fetus if pregnancy occurs while taking pomalidomide. These guidelines are outlined in the section on birth control below.

During the first cycle of therapy, we will conduct studies to measure the levels of pomalidomide in your blood at two time points: first the day you start taking the medicine, and again after you

have been taking the medicine for 2 weeks. On those days, you will have blood drawn immediately before you take the pomalidomide tablets, again at 1, 2, 3, 4, 6 and 8 hours after taking the tablets, and once more 24 hours after taking the tablets (the next morning). You do not need to be in hospital overnight for these blood draws. Each of these blood draws is less than 1½ teaspoons of blood. A small catheter (plastic tube) may be placed in your vein so that you do not have to have a new needle put into your vein for each of the blood draws.

You will be evaluated throughout the study to record any changes in your KS lesions and to ensure that you are not experiencing any intolerable side effects. During the first cycle of therapy, you will be evaluated by a physician prior to therapy, as well as two weeks later, to answer any questions you may have and to ensure that you are tolerating the therapy. On subsequent cycles, a physician will evaluate you on the day you start the pomalidomide and you will have further blood tests on that day. The blood tests include counts of blood cells, tests of blood chemistry and, for people with HIV, tests of HIV viral load and CD4 counts. For the first cycle you will have blood tests each week, and for the second and third cycles only, you will also have blood tests two weeks into the cycle to ensure you are tolerating the therapy. During clinic visits you will be asked questions to help us determine how well you are tolerating the treatment and a physical examination will be performed. Every four weeks while you are receiving the pomalidomide, you will also have an assessment of your KS lesions. If you have more than 50 KS lesions on your skin, then this assessment will focus on only a portion of your body. You will also have photographs taken of your lesions. In addition, three experimental non-invasive imaging studies will be performed. None of these will treat the KS or make it improve, and we do not believe that any of them will harm your skin. The three methods are called:

1) Laser Doppler imaging:

The laser light used for the laser Doppler can harm your eyes if you stare at it directly, but precautions will be taken so that you will not stare at it. Laser Doppler imaging takes about 3 minutes to perform on each lesion. It uses a low power laser beam that scans across the skin lesion being measured. The instrument does not touch your skin. You may be asked to have a blood pressure cuff put on your arm and have laser Doppler imaging performed before and after the cuff is inflated for a short time (generally less than thirty seconds). In standard practice, a similar machine is used to measure how deeply severe burns affect the skin and to assess allergic responses in the skin. However, its use in Kaposi's sarcoma is experimental. The purpose of this experimental use is to attempt to measure the amount of blood flow through the blood vessels in the Kaposi's sarcoma lesions.

2) Multi-spectral imaging:

The multi-spectral imaging exam should take about 2 minutes to perform on each lesion. It uses principles of the way hemoglobin absorbs light. Hemoglobin is a protein in the blood that carries oxygen to your tissues. The light on the multi-spectral imaging instrument is absorbed differently depending on whether the hemoglobin has oxygen attached to it or not. This will allow an estimate to be made regarding the total blood volume, and how much of it is carrying oxygen or not.

3) Infrared thermal imaging:

The thermal imaging takes about a minute to perform on each lesion. It uses a special camera to take digital infrared pictures of your skin. This enables us to form a picture of the temperature of your KS lesions and thus assess the blood flow in the Kaposi's sarcoma lesions.

The conventional photography and experimental imaging studies will be performed before the first cycle and then repeated after each of the first six cycles; if you receive more than six cycles the studies will be repeated every other cycle after the first six (on the odd-numbered cycles, starting with cycle 7); and the studies will be repeated again after the last cycle of therapy.

Throughout the study, we will be collecting samples from you in order to conduct additional research studies described below. A few days before you begin taking pomalidomide we will collect approximately 80 mL of blood (a little more than five tablespoons). Starting from day of cycle one, we will collect a sample of saliva and approximately 80-90mL of blood on the first day of each cycle and the last day of the final cycle (day 29). There will be additional collection of approximately 40-50 mL (around 3 tablespoons) of blood on the first day of cycles 1 and 4 and the fifteenth day of cycle 1. On the fifteenth days of cycle two and three there will be draws of 8ml (half a tablespoon) only. Finally, at your post therapy visit which will occur approximately 4 weeks after you have completed your final cycle, we will collect an additional 120mL (8 tablespoons) of blood.

We will use these samples to test for the levels of the virus that causes KS (KSHV), HIV levels if you are HIV positive, and the levels of a number of blood chemicals called cytokines that can tell us how your body and your immune system are responding to the pomalidomide.

In addition to collecting blood and saliva for research, we will ask you for permission to collect one biopsy for research while you are taking pomalidomide. Before your third cycle, you will be asked if you are willing to have a skin (lesion) biopsy for special research studies evaluating the effect of pomalidomide on your KS lesions. Additional biopsies may be taken for clinically indicated purposes. For example, when it appears that all of the KS is gone, a biopsy helps determine if there is any KS that remains, or if it is in fact completely gone. Another example is if new lesions appear while you are on therapy and they are suspicious for KS, a biopsy can be taken to determine if KS is present in the new lesion (s). These biopsies may also be used for special research studies, but their main purpose would be to determine the status of the KS. You may refuse to have the research biopsy or any of the clinical biopsies and continue to participate on the study.

When you are finished taking the drugs (treatment)

When you are finished taking the drugs, we will continue to follow you in clinic for up to five years to make sure that your KS does not return or get worse and to assess for any late side effects from the pomalidomide.

If during this time you again develop KS that requires treatment and you along with your physician agree that you may benefit from a second (optional) course of therapy with pomalidomide, you will be evaluated throughout the second course in the same manner and at the same frequency as described above, with two exceptions: blood levels of pomalidomide will not be tested during the second course and the skin biopsies for research will not be repeated during the second course. The purpose of these evaluations is to record any changes in your KS lesions and to ensure that you are not experiencing any intolerable side effects.

Study Chart

This chart outlines what will happen if you choose to participate:

Screening for Eligibility

- Medical History and Physical Exam
- Review of Biopsy
- Blood Tests
- Chest X-Ray and EKG

Treatment

Therapy:	Pomalidomide tablets each day for three weeks (21 days), followed by a one week (7 day) "rest" from the tablets
Monitoring:	Review of side effects
	Physical Exam
	Blood Tests
	Tumor measurements and photography
Research:	Blood and saliva samples
	Additional biopsy (optional)
	Non-invasive imaging
Stop treatment:	Completion of six to twelve cycles of therapy
	Progressive KS or complete resolution of KS
	Patient preference

After Treatment

- Research blood and saliva samples
- Additional biopsy (optional)
- Clinic visit every 3-6 months for first 2 years after therapy and then every year for up to 5 years
- May potentially receive a second course of pomalidomide (6-12 months) if KS again requires treatment, and if there was a benefit from the first course.

Birth Control

Pregnancy:

In addition, all patients taking pomalidomide must follow guidelines for prevention of pregnancy. This is because there is a risk of harm to a fetus if pregnancy occurs while taking pomalidomide. These guidelines are outlined below.

Screening:

- Pregnancy test, if applicable:

  If you are a female of childbearing potential*, you will be required to have two negative pregnancy tests: the first test within 10-14 days before starting pomalidomide and the second test within 24 hours before your first dose of pomalidomide.

  * For the purposes of this study, a female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or 2) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time during the preceding 24 consecutive months).

Pomalidomide was found to cause birth defects in an experimental study in animals. Pomalidomide is related to thalidomide. Thalidomide is known to cause severe life-threatening human birth defects. Pomalidomide is therefore considered to have the potential to cause birth defects in humans. If pomalidomide is taken during pregnancy, it may cause birth defects or death to an unborn baby. Females must not become pregnant while taking pomalidomide.

You have been informed that the risk of birth defects is unknown. If you are female, you agree not to become pregnant while taking pomalidomide.

In order to participate in this study you must register into and follow the requirements of the POMALYST REMS™ program of Celgene Corporation. This program provides education and counseling on the risks of fetal exposure, blood clots and reduced blood counts. You will be required to receive counseling, follow the pregnancy testing and birth control requirements of the program that are appropriate for you and take surveys regarding your compliance with the POMALYST REMS™ program.

Females:

If you are a female, you must not be pregnant.

You will be considered not of child bearing potential if you meet the following criteria:

- absence of menstrual periods (natural menopause) for the past 24 consecutive months or
- have had a hysterectomy (the surgical removal of the uterus) or both ovaries surgically removed

If you do not meet these criteria, you will be considered a female of child bearing potential. If there is ANY chance that you can become pregnant, you must follow the guidelines below.

If you **ARE** a female of childbearing potential (FCBP), you will not be able to participate in this research study unless you have had two negative pregnancy tests, one within 10-14 days and one within 24 hours of starting pomalidomide.

In addition, with your doctor's knowledge and approval, you agree to use **TWO** reliable forms of birth control or practice complete abstinence from heterosexual intercourse during the following time periods related to this study:

- for at least 28 days before starting pomalidomide
- while participating in this study
- during dose interruptions
- and for at least 28 days after discontinuation from the study

You agree to inform the investigator immediately if:

- you have any reason to suspect you are pregnant
- you find that circumstances have changed and that there is a risk of becoming pregnant
- you have stopped using the approved forms of **TWO** reliable birth control methods.
- you must talk to your doctor before changing any birth control methods.

The following methods of birth control are considered acceptable birth control methods:

Highly Effective Methods	Additional Effective Methods
Intrauterine device (IUD)	Latex condom
Hormonal (birth control pills, injections, implants)	Diaphragm
Tubal ligation	Cervical Cap
Partner's vasectomy	

Special Note: Certain HIV-protease inhibitors, griseofulvin, modafinil, pencillins, rifampin, rifabutin, phenytoin, carbamazepine, or certain herbal supplements such as St. John's Wort may reduce the effectiveness of hormonal contraceptives during and up to one month after discontinuation of these concomitant therapies.

Therefore, females of childbearing potential requiring treatment with one or more of these drugs must choose ONE non-hormonal method as the highly effective method of birth control (IUD, tubal ligation, partner's vasectomy) along with ONE of the additional effective methods (latex condom, diaphragm, cervical cap) or abstain from heterosexual contact while taking pomalidomide.

You must use at least one highly effective method and one additional effective method of birth control **AT THE SAME TIME**. However, your doctor may recommend that you use two barrier methods for medical reasons.

If you have sex without using **TWO** reliable methods of birth control, or if for any reason you think you may be pregnant, you must **IMMEDIATELY** stop taking pomalidomide and tell your doctor.

You will have pregnancy tests before and during treatment, even if you agree not to have reproductive heterosexual intercourse. You will have a pregnancy test done by the doctor every week during the first 28 days of this study. You will then have a pregnancy test every 28 days

during your participation in this study if your menstrual cycles are regular or every 14 days if your cycles are irregular. You will also have a pregnancy test if you miss your period or have unusual menstrual bleeding. In addition, you will have pregnancy tests when you are discontinued from the study and at day 28 after discontinuation from the study if your menstrual cycles are regular. If your menstrual cycles are irregular, you will have pregnancy tests when you are discontinued from the study and at days 14 and 28 after discontinuation from the study.

You must not breastfeed a baby while you are participating in this study and for at least 28 days after you have stopped taking pomalidomide.

You must **NEVER** share pomalidomide (or other study drugs) with someone else. 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. You will be counseled at least every 28 days and at discontinuation from the trial about not sharing pomalidomide (and other study drugs), the potential risks of fetal exposure, and abstaining from blood and donations.

If you have any reason to suspect you are pregnant, you must IMMEDIATELY stop taking pomalidomide and tell your doctor. If you have a positive pregnancy test while participating in this study, you must **IMMEDIATELY** stop taking pomalidomide and tell your study doctor. If you have a positive pregnancy test within 28 days after you have been discontinued from this study, you must **IMMEDIATELY** tell your doctor.

Study subjects who become pregnant will be monitored throughout the pregnancy and will continue to be monitored for 30 days after delivery (premature delivery, aborted fetus, full-term pregnancy, or no longer pregnant).

Males:

You have been informed about the risk of birth defects and you agree to use a latex condom every time you have sex with a female of childbearing potential while you are participating in this study and for at least 28 days after you have been discontinued from the study, even if you have had a successful vasectomy. You must tell your doctor if you have sex with a female of childbearing potential without using a latex condom or if you think for any reason your partner may be pregnant.

You must **NEVER** share pomalidomide (or other study drugs) with someone else. You must **NEVER** donate blood, sperm, or semen while you are participating in this study and for at least 28 days after you have been discontinued from the study. You will be counseled at least every 28 days regarding abstaining from donating blood, sperm, or semen; birth control requirements; not sharing pomalidomide (and other study drugs); and the potential risks of fetal exposure.

Risks or Discomforts of Participation

What side effects or risks can I expect from being in this study?

There is always a risk involved in taking any drugs, but you will be carefully monitored for any problems and you are encouraged to report anything that is bothering you. There may be risks or side effects of the study drug that are unknown or cannot be predicted at this time. You should not hesitate to report anything that upsets you or may be troubling you to your study physician, even if you do not think it is connected to taking the study drug. If you have any questions you should contact the study physician or member of the study team. In addition, you will receive any new information during the course of the study concerning significant treatment findings from this

study or others (good or bad) that may affect your willingness to continue your participation. In addition to the risks of the study drug, pomalidomide, described below you may experience discomfort associated with blood draws and tissue biopsies (whether clinically indicated or related to research) while participating in the study.

Risks of pomalidomide (CC-4047):

Pomalidomide (CC-4047) has been studied in healthy volunteers and in patients with cancer of the blood and other organs of the body, including Kaposi sarcoma, as well as in patients with other diseases. As with any other experimental treatment there may be side effects or risks associated with pomalidomide, some of which are not yet known. As of 12 May 2014, there were 11 completed clinical studies and 44 ongoing studies using pomalidomide, and the risks below are drawn from reports from these patients.

The side effects that patients had after starting the study drug in completed and ongoing studies are noted below. In some cases, side effects can be serious, long-lasting or may never go away, or can cause death. It is not yet possible to know for certain which of the reported side effects are directly due to pomalidomide itself. As pomalidomide is being studied as a treatment for serious diseases, some of the reported conditions could be a consequence of the disease itself, or other pre-existing diseases, or other drugs the patient may have been taking. It should not therefore be assumed that all the side effects listed below were caused by pomalidomide.

Pomalidomide can cause a decrease in the number of white blood cells, red blood cells, platelets, and/or neutrophils (a type of white blood cell). White blood cells are cells of your immune system. In some patients, a decrease in blood cells can be serious and may require you to stop treatment. A decrease in white blood cells and/or neutrophils may lead to fever and/or a life-threatening infection. The red blood cells carry oxygen to your organs. A decrease in red blood cells can lead to fatigue or feeling tired. A decrease in platelets may lead to bleeding and require stopping treatment. Other laboratory values may become abnormal, as well.

The side effects listed below are grouped as follows: 1) side effects reported in 10-46% of patients; 2) side effects reported in 1-10% of patients; and 3) other important side effects.

1) Side effects reported in 10-46% of patients participating in Celgene-sponsored clinical studies with pomalidomide included:
    - Neutropenia (low white blood cell count) with or without infection
    - Thrombocytopenia (low platelet count)
    - Anemia (a decrease in your red blood cells which carry oxygen)
    - Fever
    - Constipation
    - Diarrhea (loose stool)
    - Decreased appetite
    - Nausea
    - Fatigue (tiredness)

- Headache
- Dizziness
- Dyspnea (shortness of breath)
- Cough
- Edema (swelling)
- Rash
- Dry skin and itch
- Muscle aches or cramps

2) Side effects reported in 1 to 10% of patients participating in Celgene-sponsored clinical studies with pomalidomide included:

- Infection
- Respiratory infection (sinus or lung infection)
- Pharyngitis (inflammation of the throat)
- Vomiting
- Abnormal shaking
- Pain in chest, back, joints or limbs (arms or legs)
- Paraesthesia (skin tingling)
- Hypoaesthesia (decreased sensitivity to touch)
- Abnormal blood test results
- Confusion
- Blurry vision
- Hypothyroidism (abnormal thyroid tests, sometimes causes fatigue, constipation, dry skin or cold intolerance)

3) Other important side effects reported in patients participating in Celgene-sponsored clinical studies with pomalidomide that are considered important enough for you to be made aware of include:

- New cancers (including acute myeloid leukemia (AML) (a cancer of the bone marrow which affects your white blood cells, adrenal carcinoma (cancer of the adrenal gland), bladder transitional cell carcinoma (cancer of the urinary bladder), renal cell carcinoma (kidney cancer), myelodysplastic syndrome (MDS: a group of diseases that affect your blood and bone marrow), skin cancers and thyroid cancer
- Inflammation of your lungs
- Renal failure (kidneys not working correctly)

Deep vein thrombosis (DVT) and pulmonary embolism (PE)

Medications in the same family of medications as pomalidomide have demonstrated an increased risk of DVT (blood clot in a larger blood vessel) and PE (a blood clot in or around the lungs) in some subjects with certain medical conditions. You will receive either a "baby" aspirin or another medicine to reduce the chance of blood clotting while you are receiving pomalidomide.

Reproductive Risks

As indicated in the section on birth control, pomalidomide is related to thalidomide, a drug known to cause severe life-threatening human birth defects. If pomalidomide is taken during pregnancy, it may cause birth defects or death to an unborn baby.

Additional precautions

Other than the patient, females who are able to become pregnant and males who are able to father a child, should not touch or handle the pomalidomide capsules.

We do not know if pomalidomide has any effect on your being able to have a child in the future, please speak with your doctor about family planning options for the future.

You must agree to abstain from donating blood or sperm while taking pomalidomide (even if you temporarily stop your medication) for at least 1 week after the last dose of pomalidomide.

While in this study, if any physician or healthcare provider, other than your study physician, prescribes medication(s) for you for another condition or reason, or you are taking any: over-the-counter medications; vitamins; herbal, holistic or homeopathic remedies, please inform the study physician or a member of the research team immediately. Please also let your study physician know all of your present and past diseases and allergies. This is important because a possible interaction with some medications, vitamins, and remedies may cause serious side effects, and/or may still be unknown.

Your health care team may give you medicines to help lessen or treat side effects. Many side effects go away soon after you stop taking study drug. In some cases, side effects can be serious, long-lasting or may never go away.

You should talk to your study physician about any side effects that you have while taking part in the study.

Optional Biopsies

A punch skin biopsy will be performed. Prior to the biopsy, you will receive local anesthesia through a small injection into the area of skin surrounding the biopsy site. One quarter-centimeter samples of KS will be removed with a needle during the skin biopsy. You may require a stitch after the biopsy. Risks of the biopsy include local oozing of blood or discomfort. Infection is a rare complication of skin biopsies. The biopsy to be performed is exclusively for research purposes and will not benefit you. It might help other people in the future

<u>You will be given the opportunity to decide whether you want to have the tumor biopsy at the time of the procedure.</u>

Risks from blood draws

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting and infection.

Risks from medical Photography

There are no risks associated with medical photography.

Potential Benefits of Participation

Are there benefits to taking part in this study?

No benefit can be promised to you for your participation in this study. We cannot predict whether you will benefit directly from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer. This study may lead to an increase in understanding of this particular approach to therapy of KS, and possibly better treatments based on results from this study for patients in the future. Potential benefits to you could include shrinking of your KS or lessening of your symptoms, such as pain and swelling, which are caused by KS. However, it is possible that you will not receive any benefit from participating.

Alternative Approaches or Treatments

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

Options for standard therapy of KS includes local administration of treatment to the lesions (if they are not too numerous or too spread out) and systemic therapies that treat the whole body.

Sometimes, patients with HIV or AIDS-related KS improve with effective antiretroviral (anti-HIV) therapy alone, without needing additional therapy specifically for the KS. If a trial of antiretroviral (anti-HIV) therapy without specific KS therapy seems reasonable in your case, the study physicians will make this recommendation. Also, some patients with mild KS that is not troubling them can be observed without specific treatment.

Local therapies include radiation therapy, which can help KS so long as the area to treat is not too large and has a good blood supply and good potential for healing. A gel that you can rub on your skin called panretin has also been approved by the US Food and Drug Administration for use in KS, and again is mainly used for small lesions. In addition, for small lesions, some types of chemotherapy can be injected directly into the lesions. Sometimes, very small lesions can be frozen off using liquid nitrogen or treated with laser therapy.

Patients with KS lesions on multiple parts of their body or different areas of their skin can be treated with systemic therapies. The Food and Drug Administration has approved two systemic therapies for KS, both of which are types of cytotoxic cancer chemotherapy given through the veins: liposomal anthracyclines (liposomal doxorubicin and liposomal daunorubicin) and paclitaxel. Other systemic therapy options include other cancer chemotherapy drugs, and interferon alpha (an immune modifying drug which is injected under the skin).

Severe KS or KS that is symptomatic and involves the vital organs, such as the lungs or intestines, usually requires chemotherapy given systemically through the veins for treatment. If your KS requires this type of treatment, then the investigators on this study will inform you of this, and tell you that it would be inappropriate to treat you on this experimental study.

A reasonable approach to consider rather than entry onto this research study would be to undergo standard therapy with one of the treatment approaches mentioned above, and the investigators at the NCI who explain the research protocol will also explain your standard medical treatment options to you.

Sometimes people with advanced HIV infection and severe KS decide that they would rather have no treatment at all, other than to be kept as comfortable as possible. The study physicians will discuss this issue with you if it appears to be a reasonable approach for you. The study physicians will provide their opinion on your prospects for benefit with standard medical treatment.

We encourage you to ask any question you have about your condition. If at any time you feel that you have not been able to ask questions or do not understand any issue, we urge you to contact any member you chose on the research team, so that your questions and concerns can be addressed.

Stopping Therapy

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

- if he/she believes that it is in your best interest
- if your disease worsens or comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- If you do not follow the instructions given to you by your study doctors and nurses, including steps to prevent getting pregnant and protecting others from pomalidomide

If this occurs, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Celgene Corporation or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study have participated in the development of pomalidomide to be used in certain diseases caused by the KSHV. Also, the National Institutes of Health and the research team for this study have developed a product (an assay for viral interleukin-6) being used in this study. This means it is possible that the results of this study could lead to payments to NIH. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of this drug or the assay.

In addition, the National Institutes of Health and the research team for this study are using a drug (pomalidomide) developed by Celgene Corporation through a joint study with your researchers and the company. The company also provides financial support for this study.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor for use in making clinical decisions. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive any payment for taking part in this study.

REIMBURSEMENT

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

On this study, the NCI will reimburse the cost for some of your expenses such as those for hotel, travel, meals. 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.

COSTS

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.

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. 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 Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

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

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from Celgene Corporation, the pharmaceutical company who produces Pomalidomide.

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

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

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

Certificate of Confidentiality

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

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

The Certificate does not protect your information when it:

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

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

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

Privacy Act

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

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for

research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Robert Yarchoan, MD, Robert.yarchoan@nih.gov, at 240-760-6075. 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: _____.