SUMMARY OF CHANGES

NCI Protocol #: 8834
Local Protocol #: OSU 10156

NCI Version Date: March 15, 2024
Protocol Date: March 15, 2024

Summary of Changes

#	Section	Page(s)	Change	Rationale
1	Header	All	Updated Header with new protocol version date	Updated header with new protocol version date to reflect the updated protocol version number.
2	**What will happen if I take part in this study?**	6-9	Section updated throughout to reflect discontinuation of research sample collection.	Study endpoints have been met.
3	What will happen if I take part in this study? and How long will I be in the study?	5, 7, 10	Corrected language regarding endpoint for Lenalidomide dosing to align with changes made in an earlier amendment.	Corrected for clarity and consistency with protocol.
4	Who can answer my questions about the study?	21	Office of Responsible Research Practices contact information updated.	Updated contact information.

The Ohio State University Consent to Participate in Research

Study Title:	Phase II study of lenalidomide to repair immune synapse response and humoral immunity in early-stage, asymptomatic chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with high-risk genomic features
Principal Investigator:	**Kerry Rogers, MD**
Sponsor:	National Cancer Institute

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. Why is this study being done?

This is a clinical trial, a type of research study. You are being asked to take part in this study because you have chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) that has never been treated. Only patients with CLL/SLL that has certain features considered to be high-risk will be asked to participate. All participants should be less than 80 years old or have special justification to participate due to the higher risk of toxicity in those older than 80 years of age. Newer blood tests better predict whether the disease is likely to worsen quickly (high-risk CLL) or is likely to remain stable or develop slowly (low-risk

CLL). If you are asked to participate in this study, your CLL has one or more high-risk features.

Even when the disease is in its early stages, patients with CLL/SLL are at increased risk for infections, including life-threatening infections like pneumonia. While there are vaccines to prevent some kinds of pneumonia, these vaccines are not very effective when given to CLL/SLL patients because of the low immunity associated with the disease. The low immunity often worsens as the CLL/SLL worsens, and some of the common medicines to treat CLL/SLL can further damage the immune system. Some studies have shown that pneumonia vaccines work best before low immunity worsens.

The purpose of this study is to determine whether vaccination for the most common type of pneumonia will work better when given early in the course of disease (before symptoms develop or treatment is required) and whether the addition of an experimental drug called lenalidomide can help the vaccine work better. Lenalidomide is a cancer treatment approved by the U.S. Food and Drug Administration (FDA) for the treatment of myelodysplastic syndrome (MDS) and multiple myeloma, but its use in CLL/SLL is considered investigational. Unlike other cancer treatments, lenalidomide appears to work by stimulating parts of the immune system to fight the cancer. When lenalidomide was given to patients with CLL/SLL in other studies, it not only decreased the number of abnormal cells in the blood and lymph nodes but also helped to reverse the associated low immunity. For this reason, giving lenalidomide along with the vaccine may improve the chance that the pneumonia vaccine will work in CLL/SLL patients.

All patients in this study will receive both lenalidomide treatment and pneumonia vaccine. The specific vaccine used in this study is Prevnar 13, a type of pneumonia vaccine which some studies show may work better in patients with low immunity, like CLL/SLL patients. While Prevnar 13 is approved by the U.S. FDA, the combination of combination of lenalidomide and Prevnar 13 vaccine for pneumonia is experimental in CLL/SLL patients.

YOU SHOULD NOT PARTICIPATE IN PREGNANCY WHILE TAKING LENALIDOMIDE. (SEE FURTHER INFORMATION BELOW)

Because the best time to begin treatment for patients with high-risk CLL/SLL is uncertain, another purpose of this study is to learn whether the drug lenalidomide will help the disease progress more slowly when started before the disease worsens and symptoms develop. We will study whether the treatment increases the time until standard chemotherapy treatment is needed and whether early treatment helps patients with the disease live longer. We also want to find out if there is a relationship between certain features of the CLL/SLL cells and whether the disease will respond to lenalidomide treatment. These features will be used to guide other treatment studies like this one in the future.

2. How many people will take part in this study?

About 50 people will take part in this study. A minimum of 22 patients will be assigned to each treatment arm to learn whether lenalidomide can help pneumonia vaccine work better and whether it is better to give lenalidomide before versus after vaccination. Additional patients may be recruited to help us better understand the chance that low-dose lenalidomide will control high-risk patients' CLL/SLL.

3. What will happen if I take part in this study?

This is a clinical trial (a type of research study). It includes only patients who choose to take part. You may take your time to make your decision and discuss this with your family and friends. By agreeing to be a part of this study, you are agreeing to comply with the study requirements.

In order to find out if you qualify for the study, you will have a medical evaluation done. A description of tests and visits required for the medical evaluation are listed below.

Pre-treatment Evaluation:

To find out if you qualify for the study, you will undergo several tests and procedures, as well as a complete medical examination. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Medical History
- You will be asked for a complete list of medicines you are taking, including supplements and vitamins.
- Physical Examination (including vital signs, height and weight, measurement of lymph nodes, liver, spleen).
- Routine Blood Tests (Complete Blood Count, test of blood chemistries – various substances in the blood, beta-2-microglobulin, direct and indirect Coombs, immunoglobulins)
- Special blood tests to find out whether you have high-risk CLL (cytogenetics, and immunoglobulin gene mutation test).
- If you are a woman of child bearing potential you will be required to complete a serum pregnancy test with negative results within 10-14 days of treatment.)
- Women of childbearing potential and men must agree to use adequate contraception for at least 14 days prior to the study and for the duration of participation.
- Electrocardiogram (EKG), a record of the electrical activity of your heart.

- A CT (computed tomography) scan will be performed to measure the size of the cancer in your body. A CT scan is a computerized x-ray that gives your doctor clearer pictures of the inside of your body. CT scans are routine procedures used to help doctors diagnose and follow the size and location of your cancer.
- Bone Marrow Biopsy and Aspirate will only be done only if your doctor thinks it is necessary.
- Urinalysis, TSH, Anti-pneumococcal antibody titers.

During the Study:

If you are eligible for this study, you will be "randomized" into one of two study groups. Randomization means that you are put into a study group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group in which you will be placed. You will have an equal chance of being placed either in "Arm A" in order to start treatment with lenalidomide 2 months before the first of two pneumonia vaccine shots ("concurrent"), or in "Arm B" to start lenalidomide treatment two months after getting the second pneumonia vaccine shot ("sequential"). Patients will be randomized in this way because it is not known whether either approach offers a benefit over the other. Arms A and B are described in detail below.

General Instructions for Taking Lenalidomide

Once it is determined that you are eligible for the study and you agree to receive treatment, you will begin therapy as described below. Regardless of the study group to which you are assigned, there are some important things you should know about taking lenalidomide.

- Swallow lenalidomide capsules whole with water at the same time each day. Do not break, chew or open the capsules.
- If you miss a dose of lenalidomide, take it as soon as you remember on the same day. If you miss taking your dose for the entire day, take your regular dose the next scheduled day (do NOT take double your regular dose to make up for the missed dose).
- If you take more than the prescribed dose of lenalidomide you should seek emergency medical care if needed and contact study staff immediately.
- Females of childbearing potential that might be caring for you should not touch the lenalidomide capsules or bottles unless they are wearing gloves.
- Patients who have a recent history of (less than 6 months) or increased risk for blood clots, either deep venous thrombosis (DVT) or pulmonary embolus (PE), will be asked to take medicine to prevent new clots from forming. Medicines commonly used for this purpose include aspirin and heparin, but the final choice will be made by you and your doctor.
- You will be asked to return any unused study drug and empty bottles to the clinic at each visit.

Arm A

Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8+
		V		**V**			
L	**L**	**L**	**L**	**L**	**L**	**L**	**L**

L = lenalidomide (taken once a day every day of the cycle)
V = PCV13 pneumonia vaccine (given on the first day of the cycle indicated)

Treatment for patients assigned to Arm A is summarized in the table above. Treatment for this study is organized into 28-day long cycles. Lenalidomide is a capsule which is taken once a day on each day of the treatment cycle. Each dose of Lenalidomide can be taken with or without food. Patients assigned to Arm A will begin treatment with lenalidomide on the first day of the first cycle and continue to take one dose on each day of the 28-day cycle. During Cycle 2, you will continue taking lenalidomide once daily, but your doctor may adjust the dose (higher or lower) based upon how well you tolerate the medicine during Cycle 1. The first dose of the Prevnar 13 pneumonia vaccine will be given as a shot into the upper arm on the first day of Cycle 3, during which you will also take lenalidomide once a day. The second dose of Prevnar 13 vaccine will be given on the first day of Cycle 5. After Cycle 5, there will be no more vaccine shots, but you will continue to take lenalidomide once a day until your disease worsens, you develop unacceptable side effects, or if you are removed from treatment for other reasons.

Laboratory testing, history, and physical examination are performed weekly during the first two weeks of Cycle 1. The same schedule of visits and lab tests will be performed during any cycle in which the dose of lenalidomide is increased.

Before starting another cycle of treatment, you will undergo the following:

- Physical Examination (vital signs, height and weight; lymph node, liver, and spleen measurements)
- You will be asked about any side effects you may have experienced.
- You will be asked about any medications that you are currently taking, including supplements and vitamins.
- Routine blood tests
- Pregnancy testing if you are a woman of childbearing potential
- All patients (men and women) will be reminded that lenalidomide may cause birth defects and that birth control must be used by all patients (men and women) enrolled on the study. Your doctor, nurse, or a study coordinator will ask you to sign a form showing that you have been told about the risks and agree to use birth control as described below (see Appendix).
- Review of a medication diary where you will record taking each daily dose of lenalidomide.
- You will be asked about any infections you may have had since your last visit

During the course of your treatment you will have many blood draws, both to medically monitor your response to lenalidomide and the pneumonia vaccine and for research purposes. The blood draws for research only are listed below. Blood draws for research purposes have been discontinued upon approval of this updated consent form.

Cycle 1

Treatment Day and Time from Taking Lenalidomide	**Approximate Amount of Blood Drawn for Research**
Day 1, before lenalidomide	6 Teaspoons
Day 3, before lenalidomide	6 Teaspoons
Day 8, before lenalidomide	6 Teaspoons

Cycle 2

Treatment Day and Time from Taking Lenalidomide	**Approximate Amount of Blood Drawn for Research**
Day 1, before lenalidomide	6 Teaspoons
Day 1, 30 minutes, 1, 2, 3, 4½ , and 6 hours after lenalidomide	1 Teaspoon of blood at each time
Day 2, before lenalidomide	1 Teaspoon

Cycles 3, 5, 6, 7, and then every 6 months you continue to receive treatment:

Treatment Day and Time from Taking Lenalidomide	**Approximate Amount of Blood Drawn for Research**
Day 1, before lenalidomide	▪ None

Arm B

Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8+
V		**V**					
			L	**L**	**L**	**L**	**L**

L = lenalidomide (taken once a day every day of the cycle)
V = PCV13 pneumonia vaccine (given on the first day of the cycle indicated)

Treatment for patients assigned to Arm B is summarized in the table above. Treatment for this study is organized into 28-day long cycles. The first dose of the Prevnar 13 pneumonia vaccine will be given as a shot into the upper arm on the first day of Cycle 1. The second dose of Prevnar 13 vaccine will be given on the first day of Cycle 3. After Cycle 3, there will be no more vaccine shots

Treatment with lenalidomide will not start until Cycle 4. Lenalidomide is a capsule which is taken once a day on each day of the treatment cycle. Each dose of Lenalidomide can be taken with or without food. Patients assigned to Arm B will

begin treatment with lenalidomide on the first day of the fourth cycle and continue to take one dose on each day of the 28-day cycle. During Cycle 5, you will continue taking lenalidomide once daily, but your doctor may adjust the dose (higher or lower) based upon how well you tolerate the medicine during Cycle 4. You will continue to take lenalidomide once a day until your disease worsens, you develop unacceptable side effects, or if you are removed from treatment for other reasons.

Because there is a risk for side effects when you start taking lenalidomide, you will undergo laboratory tests every day for the first five days of lenalidomide treatment before you take each day's dose. You will also be asked about symptoms and side effects and undergo a brief physical examination on the first, third, and fifth day of treatment. Laboratory testing, history, and physical examination are performed weekly during the rest of Cycle 4. The same schedule of lab tests will be performed during any later cycle in which the dose of lenalidomide is increased.

Before starting another cycle of treatment, you will undergo the following:

- Physical Examination (vital signs, height and weight; lymph node, liver, and spleen measurements)
- You will be asked about any side effects you may have experienced.
- You will be asked about any medications that you are currently taking, including supplements and vitamins.
- You will be asked about any infections you may have had since your last visit.
- Routine blood tests
- Pregnancy testing if you are a woman of childbearing potential
- All patients (men and women) will be reminded that lenalidomide could cause birth defects and that birth control must be used by all patients (men and women) enrolled on the study. Your doctor, nurse, or a study coordinator will ask you to sign a form showing that you have been told about the risks and agree to use birth control as described below (see Appendix).
- Review of a medication diary where you will record taking each daily dose of lenalidomide.

During the course of your treatment you will have many blood draws, both to medically monitor your response to lenalidomide and the pneumonia vaccine and for research purposes. The blood draws for research only are listed below. Blood draws for research purposes have been discontinued upon approval of this updated consent form.

Cycle 4

Treatment Day and Time from Taking Lenalidomide	**Approximate Amount of Blood Drawn for Research**
Day 1, before lenalidomide	6 Teaspoons
Day 3, before lenalidomide	6 Teaspoons

Day 8, before lenalidomide	6 Teaspoons

Cycle 5

Treatment Day and Time from Taking Lenalidomide	Approximate Amount of Blood Drawn for Research
Day 1, before lenalidomide	6 Teaspoons
Day 1, 30 minutes, 1, 2, 3, 4½ , and 6 hours after lenalidomide	1 Teaspoon of blood at each time
Day 2, before lenalidomide	1 Teaspoon

Cycles 1, 3, 6, 7, and then every 6 months you continue to receive treatment:

Treatment Day and Time from Taking Lenalidomide	Approximate Amount of Blood Drawn for Research
Day 1, before lenalidomide (Cycle 7+)	▪ None

Both Arm A and Arm B

During treatment you may also receive additional medications to prevent or treat side effects:

- Unless allergic, all patients will receive a daily dose of allopurinol beginning at least three days before and continuing for at least one month after starting lenalidomide. This medication is used to prevent a serious group of signs and symptoms due to rapid breakdown of tumor that can rarely occur after lenalidomide treatment has started.
- Some patients taking lenalidomide experience temporary growth in tumor or worsening of tumor related problems soon after they start taking the medicine. If this happens, your doctor may prescribe dexamethasone, a steroid medicine, which previous studies have shown can help this problem.

After you complete treatment, you will undergo additional testing to find out if lenalidomide helped the pneumonia vaccine work better and how well the lenalidomide worked to control your disease:

- Physical Examination (vital signs, height and weight; lymph node, liver, and spleen measurements)
- You will be asked about any side effects you may have experienced.
- You will be asked about any medications that you are currently taking, including supplements and vitamins.
- You will be asked about any infections you may have had since your last visit.
- Routine Blood Tests (Complete Blood Count, test of blood chemistries – various substances in the blood, direct and indirect Coombs, immunoglobulins,, and liver function tests.)
- Tumor Measurement (either a MRI or CT Scan)*
- Bone Marrow Biopsy and Aspirate *

**Your doctor might also decide to do these tests earlier if he or she thinks that all signs of the disease are gone, which is called "remission."*

After you finish treatment, you will be followed on a long-term basis. Follow-up visits are scheduled every 3 months during the first year and every 6 months for the following years. You will be followed as part of this study until you decide to no longer take part or you start another treatment for your disease. At each follow-up visit, your doctor will do the following:

- Physical Examination (vital signs, height and weight; lymph node, liver, and spleen measurements).
- You will be asked about any side effects you may have experienced.
- You will be asked about any medications that you are currently taking, including supplements and vitamins.
- You will be asked about any infections you may have had since your last visit.
- Routine Blood Tests (Complete Blood Count, test of blood chemistries – various substances in the blood, direct and indirect Coombs, immunoglobulins, and liver function tests.)
- Tumor Measurement (either a MRI or CT Scan), if your doctor feels it is necessary.
- Bone Marrow Biopsy and Aspirate, if your doctor feels it is necessary.

4. How long will I be in the study?

You may continue to receive lenalidomide until your disease worsens, you develop unacceptable side effects, or until you are removed from treatment for other reasons.. After you complete your treatment with lenalidomide, we would like to continue keeping track of your medical condition. As outlined above, you will be seen and examined by your doctor every 3 months during the first year after stopping lenalidomide treatment and every 6 months thereafter. Your doctor will monitor how well your disease responded to this treatment, to make sure that any side effects have resolved, and to find out if you have developed any unexpected side effects. Your doctor will also want to know about any infections you have had since your last visit. You will be encouraged to follow-up as part of this study until you decide to no longer take part or you start another treatment for your disease.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Tell your doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely. It is important to tell your doctor if you are thinking about stopping so that any risks from the vaccine or lenalidomide treatment can be evaluated. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could

be most helpful to you. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

If you choose to take part in this study, there is a risk that the lenalidomide (CC-5013**)** 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 lenalidomide (CC-5013) 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 be testing 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.

A. Prevnar 13 (Pneumococcal 13-Valent Vaccine, Diphtheria Conjugate)

Common

- Pain at the injection site
- Redness at injection site.
- Swelling at injection site.
- Tenderness at injection site
- Loss of appetite
- Insomnia
- Sleepiness
- Irritability
- Fever

Uncommon But Serious (<2% of patients)

- a painful, red skin rash that typically occurs on the lower legs
- allergic reaction that can cause severe problems with breathing and/or changes in blood pressure and heart rate
- hypersensitivity reaction (rash, itching, and shortness of breath)
- swelling of lymph nodes near the site of the injection
- seizures, which have only been reported in very young children with fever
- irritability
- Respiratory tract infections
- difficulty breathing
- swelling, including severe swelling of the face and/or tongue

B. Lenalidomide

COMMON, SOME MAY BE SERIOUS In 100 people receiving lenalidomide (CC-5013), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Constipation, diarrhea • Tiredness • Bruising, bleeding

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving lenalidomide (CC-5013), from 4 to 20 may have:

- Infection, especially when white blood cell count is low
- Dizziness, fainting
- Blurred vision
- Cloudiness of the eye, visual disturbances
- Pain
- Dry mouth, skin
- Heartburn, nausea, vomiting
- Chills, fever
- Swelling of the body
- Fall
- Weight loss, loss of appetite
- Dehydration
- Muscle weakness
- Abnormal unpleasant sensation, body movement
- Changes in taste
- Headache
- Feeling of "pins and needles" in arms and legs
- Numbness, tingling or pain of the arms and legs
- Depression
- Difficulty sleeping
- Change in mood
- Cough, shortness of breath
- Nose bleed
- Increased sweating
- Itching, rash
- Sores on the skin
- High blood pressure which may cause headaches, dizziness, blurred vision
- Low blood pressure which may cause feeling faint
- Blood clot which may cause swelling, pain, shortness of breath

RARE, AND SERIOUS

In 100 people receiving lenalidomide (CC-5013), 3 or fewer may have:

- Abnormal heartbeat
- Heart attack, heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Liver damage which may cause yellowing of eyes and skin, swelling
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Damage to organs in the body when donor cells attack host organs
- Kidney damage which may require dialysis
- Damage to muscle which may cause muscle pain, dark red urine
- Cancer of bone marrow caused by chemotherapy
- Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions
- Increased tumor size
- A new cancer unrelated to an earlier cancer
- A new cancer resulting from treatment of earlier cancer
- Stroke which may cause paralysis, weakness
- Damage to the lungs which may cause shortness of breath
- Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body
- Difficulty stimulating enough stem cells in the bloodstream for future transplant

These potential risks have been associated with Lenalidomide but the relationship is still undetermined:

- Meningitis (an inflammation of the covering around the spinal cord and brain that is possibly life threatening)
- Leukoencephalopathy (progressive damage to the brain)
- Pancreatitis (inflammation of the pancreas)

C. Allopurinol

Common:

- skin rash
- diarrhea
- nausea or urge to vomit
- gout flare, in patients with a history of that condition
- itching
- hives
- sleepiness

- Elevated Liver Function Tests (an increase in the blood levels of liver enzymes (ALT/AST) that measure how well the liver is working and may mean damage to the liver has happened)
- increased number of a type of white blood cell (eosinophil) associated with allergic reactions

Rare but serious:

- hair loss
- bruising
- irritation and/or inflammation of blood vessels
- decreased number of a type of white blood cells (neutrophil/granulocyte), which may increase the risk for infection
- decreased number of blood cells that help blood to clot (platelets), which may increase the risk for bleeding
- lack of enough red blood cells (anemia)
- injury to the liver
- injury to the kidney
- change in sensation or injury to nerves responsible for sensation
- seizures

C. Dexamethasone

- Difficulty sleeping (insomnia)
- Appetite change
- Dizziness
- Headache
- Anxiety or restlessness
- Heartburn or indigestion
- Edema (mild accumulation of fluid in your body)
- Mood swings, nervousness or depression
- Elevated blood sugar
- Acne
- "Flushing" (red cheeks or feeling of warmth on your face)
- Low or high potassium blood levels
- Severe allergic reaction (rare)
- Adrenal insufficiency (rare condition in which the adrenal glands, located above the kidneys, do not produce adequate amounts of steroid hormones)
- Congestive heart failure (Rare condition where the heart becomes weak and loses its pumping ability)
- Changes in blood pressure
- Muscle weakness
- Vision changes
- Sweating
- Slower wound healing

D. Risks Associated with Pregnancy

Lenalidomide is related to thalidomide. Thalidomide is known to cause severe life-threatening human birth defects. Findings from a monkey study indicate that lenalidomide caused birth defects in the babies of female monkeys who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to any unborn baby. Women must not become pregnant while taking lenalidomide. You have been informed that the risk of birth defects is unknown. If you are female, you agree not to become pregnant while taking lenalidomide.

Patients who take lenalidomide and dexamethasone have a greater chance of having blood clots. Because of this, it is recommended patients not take birth control pills or hormone replacement therapy before discussing with the doctor and considering the risks and benefits of these choices.

When taking lenalidomide, the drug is present in semen of healthy men at very low levels for three days after stopping the drug. For patients who may not be able to get rid of the drug, such as people with kidney problems, lenalidomide may be present for more than three days. To be safe, all men should use condoms when engaging in sexual intercourse while taking lenalidomide, when temporarily stopping lenalidomide, and for 28 days after permanently stopping lenalidomide treatment if their partner is either pregnant or able to have children.
Patients should not donate blood during study treatment or for 28 days following discontinuation of lenalidomide.

You will be counseled at least every 28 days during lenalidomide treatment and again one last time when you stop taking lenalidomide about not sharing lenalidomide (or other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the "Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies" with each new supply of lenalidomide as a reminder of these safety issues.

E. Risks Associated with Study Procedures

Blood drawing risks:
There may be bruising, bleeding or inflammation at the sites where blood samples are taken. Care will be provided to avoid these complications.

Bone Marrow Biopsy risks:

Complications related to bone marrow aspirations and biopsies may include bleeding (inside or outside the body), pain, bruising, blood clots and infection. Care will be taken to avoid these complications.

Imaging (CT scans):
The known risks associated with CT scans include the rare occurrence of allergic reactions to the contrast dyes injected into a vein during the scan. Such allergic reactions can involve itching, rash, or in severe cases, difficulty in breathing and dangerous lowering of blood pressure. If you have known allergic reactions to imaging contrast agents, you should let your study doctor and radiologist know. Additionally, these scans are associated with exposure to very small amounts of radiation.

For more information about risks and side effects of these or any other tests and procedures, always ask your doctor or another member of your health care team.

7. What benefits can I expect from being in the study?

There is no guarantee that this treatment will benefit you. This treatment regimen may also be harmful to you. However, the benefits could be a better response to pneumonia vaccine and a decreased risk of getting pneumonia caused by the common pneumonia germ that the vaccine targets. Other possible benefits include improved immunity to other infections, a longer time to developing symptoms from the disease, longer freedom from disease-related symptoms, and/or increased survival. This study may also increase knowledge about both lenalidomide and vaccine treatment in patients with high-risk CLL/SLL, which should benefit other patients in the future.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled. If you choose not to participate in this trial, other treatments you qualify for will be discussed with you. Your other choices may include:

- Receiving the pneumonia vaccine without taking part in a study
- Getting treatment or care for your CLL/SLL without being in a study.
- Taking part in another study for CLL.
- Getting no treatment.

Talk to your doctor about your choices before you decide if you will take part in this study.

9. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies involved in keeping research safe for people;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The National Cancer Institute (NCI)
- Pharmaceutical Collaborator (makers of lenalidomide), the manufacturer of lenalidomide who has agreed to cooperate with the NCI to study the drug in patients with CLL/SLL;
- Your insurance company (if charges are billed to insurance).

The National Cancer Institute will obtain information from this clinical trial under data collection authority Title 42 U.S.C. 285

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

Your research specimens will be kept in a secure lab that only permits authorized persons to enter. Persons having access to your samples are the principal investigator and all authorized laboratory personnel. Your samples will be used to analyze how this treatment works in the body.

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.

10. What are the costs of taking part in this study?

Under normal circumstances you would have physician appointments and undergo similar lab and scan procedures on the same schedule. It is known as standard of care, and therefore you and/or your insurance company will be billed for the physician visits, various blood tests, CT scans, bone marrow biopsy and aspirate and medication treatments given before and while being treated with lenalidomide. You will be responsible for co-pay/deductible required by your insurance plan while on study.

The tests that are exclusively done for the research will not be billed to your insurance company. These research tests include research blood draws and laboratory testing done on the specimens noted above in section 3.

The NCI will provide the lenalidomide at no charge while you take part in this study. The NCI does not cover the cost of getting the lenalidomide and giving it to you, so you or your insurance company may have to pay for this. The pneumonia vaccine (Prevnar13) is commercially available, so the cost of the vaccine will be billed to your insurance company. You will be responsible for co-pay/deductible required by your insurance plan.

Even though it probably will not happen, it is possible that the NCI may not be able to continue to provide the lenalidomide for some reason. If this would happen, the study may have to close. Your study doctor will talk with you about this, if it happens.

This study requires the following research- related tests which will also be covered by the study and will not be billed to you or your insurance company:

- Anti-pnemococcal antibody titers which measure how well the pneumonia vaccine will work to prevent infection
- Pharmacokinetics which study the drug levels within the body and how the body metabolizes the drug.
- Pharmacodynamics which study the effects of the drugs within the body and on cancer cells

All other tests and procedures are considered standard of care. This means that you would have done these for your regular cancer care. **You or your insurance company will pay for these regular tests and procedures.**

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

11. Will I be paid for taking part in this study?

You will not be paid to take part in this study. If you choose to take part in this study, it will be on a voluntary basis.

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

13. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact **Dr. Kerry Rogers at 614-293-3196.**

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact **Dr. Kerry Rogers** at **614-293-3196.**

APPENDIX: Reproductive Risks Associated with Lenalidomide

Lenalidomide is related to thalidomide. Thalidomide is known to cause severe life-threatening human birth defects. Findings from a monkey study indicate that lenalidomide caused birth defects in the offspring of female monkeys who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to an unborn baby. Females must not become pregnant while taking lenalidomide. If you are female, you agree not to become pregnant while taking lenalidomide. Lenalidomide is present at very low levels in human semen of healthy men for three days after stopping the drug according to a study. For some men, such as men with kidney problems, lenalidomide may be present in semen for more than three days. Because of the risk of birth defects, all patients taking lenalidomide must read the following statements that apply to you according to your gender and menopausal status.

IF YOU ARE A FEMALE WHO *IS ABLE* TO BECOME PREGNANT*

*(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 (not having menstrual cycles due to cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time during the preceding 24 consecutive months)

Please read thoroughly and initial each space provided if you understand each statement:

_____: You understand that birth defects may occur with the use of lenalidomide. You have been warned by your doctor that your unborn baby may have birth defects and can even die, if you are pregnant or become pregnant while taking lenalidomide.

_____: You understand that you must NOT take lenalidomide if you are pregnant, breast-feeding a baby or able to get pregnant and not using 2 reliable methods of birth control.

_____: If you are having sexual relations with a man, your uterus and/or both ovaries have not been removed, you have had at least one menstrual period in the past 24 months and/or your menses stopped due to treatment of your disease, you understand that you are able to become pregnant. You must use one highly effective method of birth control plus one additional effective method of birth control (contraception) at the SAME TIME.

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	

_____: These birth control methods must be used during the following time periods related to this study: 1) for at least 28 days before starting therapy; 2) while participating in the study; during interruptions in therapy and 3) for at least 28 days after lenalidomide has been stopped. You must use these methods unless you completely abstain from heterosexual sexual contact. If a hormone (birth control pill, injection, patch or implant) or IUD method is not medically possible for you, you may use another highly effective method or two barrier methods AT THE SAME TIME.

_____:You know you must have a pregnancy test done by your doctor within 10 – 14 days and again within 24 hours prior to starting lenalidomide therapy, even if you have not had your menses due to treatment of your disease or had as little as one menstrual period in the past 24 months. If you have regular or no menstrual cycles, you will then have pregnancy tests every week for the first 28 days, then every 28 days while you are taking lenalidomide, again when you have been taken off of lenalidomide therapy and then 28 days after you have stopped taking lenalidomide. If you have irregular menstrual cycles, you will have pregnancy tests every week for the first 28 days, then every 14 days while you are taking lenalidomide, again when you have been taken off of lenalidomide therapy, and then 14 days and 28 days after you have stopped taking lenalidomide.

_____: You know you must immediately stop taking lenalidomide and inform your doctor, if you become pregnant while taking the drug, if you miss your menstrual period or have unusual menstrual bleeding, if you stop using 2 reliable forms of birth control, or if you think for any reason that you may be pregnant. You must talk to my doctor before changing any birth control methods.

_____: You are not now pregnant, nor will you try to become pregnant for at least 28 days after you have completely finished taking lenalidomide.

_____: You understand that lenalidomide will be prescribed only for you. You must not share it with ANYONE, even someone that has similar symptoms to yours. It must be kept out of reach of children and should never be given to females who are pregnant or able to have children.

_____: You agree any unused drug supply will be returned to the research site at each visit.

_____: You know that you cannot donate blood while taking lenalidomide and for 28 days after stopping lenalidomide.

Study patients 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).

IF YOU ARE A MALE

Please read thoroughly and initial each space provided if you understand each statement:

_____: You understand that birth defects may occur with the use of lenalidomide. You have been warned by my doctor that an unborn baby may have birth defects and can even die, if a female is pregnant or becomes pregnant while taking lenalidomide.

_____: You have been told by my doctor that you must NEVER have unprotected sexual contact with a female who can become pregnant. Because lenalidomide is present in semen, your doctor has explained that you must completely abstain from sexual contact with females who are pregnant or able to become pregnant, or you must use a latex condom every time you engage in any sexual contact with females who are pregnant or may become pregnant. You must do this while you are taking lenalidomide and for 28 days after you stop taking lenalidomide, even if you have had a successful vasectomy.

_____: You know you must inform my doctor if you have unprotected sexual contact with a female who is pregnant or can become pregnant or if you think, for ANY REASON, that your sexual partner may be pregnant. Female partners of male patients taking lenalidomide should be advised to call their own physician immediately if they get pregnant.

_____: You understand that lenalidomide will be prescribed only for me. You must not share it with ANYONE, even someone that has similar symptoms to yours. It must be kept out of reach of children and should never be given to females who are able to have children.

_____: You agree any unused drug supply will be returned to the research site at each visit.

_____: You know that you cannot donate blood, sperm or semen while taking lenalidomide for 28 days after stopping lenalidomide.

IF YOU ARE A FEMALE THAT IS *NOT* ABLE TO BECOME PREGNANT

Please read thoroughly and initial each space provided if you understand each statement:

_____: You understand that birth defects may occur with the use of lenalidomide. You have been warned by your doctor that an unborn baby may have birth defects and can even die, if a female is pregnant or becomes pregnant while taking lenalidomide.

_____: You certify that you are not now pregnant, nor are you of child bearing potential as you have been in a natural menopause for at least 24 months (been through the change in life without even 1 (one) menstrual period for the past 24 months); or you had my uterus removed (hysterectomy) or had both your ovaries removed (bilateral oophorectomy).

_____: You understand that lenalidomide will be prescribed only for you. You must not share it with ANYONE, even someone that has similar symptoms to yours. It must be kept out of reach of children and should never be given to females who are pregnant or able to have children

.

_____: You agree any unused drug supply will be returned to the research site at each visit.

_____: You know that you cannot donate blood while taking lenalidomide and for 28 days after stopping lenalidomide.

ALL PARTICIPANTS

You will be counseled at least every cycle during lenalidomide administration and again when you stop taking lenalidomide about not sharing lenalidomide (and other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the "**Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies**" with each new supply of lenalidomide as a reminder of these safety issues.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form**.**

Printed name of subject	**Signature of subject**
	AM/PM
	Date and time
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)**
Relationship to the subject	**AM/PM**
	Date and time

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time