

Title: Duvelisib for Ibrutinib-Resistant Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

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PRINCIPAL INVESTIGATOR: Clare Sun, MD

STUDY TITLE: Duvelisib for Ibrutinib-Resistant Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

STUDY SITE: National Heart, Lung, and Blood Institute

Cohort: Affected patient

Consent Version: *Consents should be versioned using the date of the last revision. Each time the consent is revised, you must update the version date. Use this space to specify the version date.*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator:

Clare Sun

clare.sun@nih.gov

301-402-1806

Research Nurse:

Pia Nierman

pia.nierman@nih.gov

301-827-1094

KEY INFORMATION ABOUT THIS RESEARCH

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

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

You are being asked to be in this research study because you have a form of cancer called chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). You have been receiving ibrutinib to treat CLL/SLL, but your CLL/SLL is no longer responding to ibrutinib or has developed mutations in certain genes that would eventually stop ibrutinib from working. We want to find out if adding another drug called duvelisib to your treatment will help your cancer.

Duvelisib is a type of drug that blocks proteins inside CLL/SLL cells. The specific protein blocked by duvelisib helps CLL/SLL cells live and grow. Laboratory studies have shown that duvelisib can kill CLL/SLL cells obtained from patients who no longer respond to ibrutinib. Drugs similar to duvelisib can control CLL/SLL in some patients who no longer respond to ibrutinib and we want to know if duvelisib has the same effect.

You will take duvelisib by mouth twice daily. Your CLL/SLL might get worse if ibrutinib is suddenly stopped. To prevent this from happening, you will continue ibrutinib at your current dose with duvelisib for the first 6 months. You will then continue duvelisib alone until your

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CLL/SLL no longer responds to duvelisib or you experience intolerable side effects from duvelisib.

You must return to the NIH monthly during the first 6 months of this study then every 3 months thereafter. Blood tests, bone marrow biopsies and CT scans will be performed periodically to see how your CLL/SLL is responding. Blood tests will also be used to monitor the safety of duvelisib. Visits will take place at the NIH Clinical Center. Most visits, including tests, will take less than a day. The study staff will provide specific dates and times for your study visits and tests.

You may continue taking most medications that were prescribed before you started the study. Because these other medicines might interact with the study drugs, we ask that you tell us about all of your medications or changes in the medications you take, including prescription drugs, over-the-counter products, vitamins, and herbal supplements.

Patients treated with duvelisib may be at an increased risk of developing certain infections. You will take an antibiotic and an antiviral medication to prevent such infections. You may also require steroids if you experience side effects related to a heightened immune system or granulocyte-colony stimulating factor if your white blood cell count decreases below normal.

Side effects occurring in more than 25 out of 100 patients treated with duvelisib for blood cancer were:

- Infections that could be caused by a bacteria, virus, or fungus.
- Frequent loose watery stools (diarrhea) and/or inflammation of the intestines (colitis).
- Decrease in number of white blood cells that helps fight infection with or without fever.
- Rash which may be itchy or may cause blisters.
- Feeling tired or weak.
- Fever.
- Cough.
- Feeling sick to your stomach

Side effects occurring in more than 10 but less than 25 out of 100 subjects treated with duvelisib for blood cancer were:

- Abnormally high level of enzymes produced by the liver meaning that it could affect how your liver functions.
- Pain in your muscles and/or joints.
- Decrease in red blood cells and decrease in cells in the blood that help the blood to clot.
- Swelling which may be in a specific location or may be more generalized.
- Decreased appetite

In addition, a small number of subjects experienced severe inflammation of the lungs which can be serious and can lead to death in rare cases (<1%).

If you have any new and concerning systemic symptoms (e.g. fevers, rigors, severe fatigue), respiratory symptoms (e.g. shortness of breath, persistent cough, chest pain), or gastrointestinal

symptoms (e.g. diarrhea or blood in your stool), you should immediately notify your doctor for further evaluation.

Your participation will continue as long as you continue to respond to and tolerate duvelisib, as long as the duvelisib remains available, until you decide that you no longer want to be in this study, or the Sponsor decides to stop or interrupt the study.

The possible benefit from this study is that duvelisib will help treat your CLL/SLL. If you decide to participate in this study, your health will be monitored very closely which may provide a benefit to you. By being in this study, you will give doctors more information about how well duvelisib works. It may help doctors understand your condition better and may help future patients with CLL/SLL.

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could choose to be treated by your home health care provider. Venetoclax (Venclexta®) is a Bcl-2 inhibitor approved for previously treated CLL/SLL. Idelalisib (Zydelig®), a PI3Kδ inhibitor, combined with rituximab (Rituxan®), a monoclonal antibody, is approved for CLL/SLL after 2 prior therapies. If you received ibrutinib as the first treatment for your CLL/SLL, chemotherapy combined with monoclonal antibody is also an option. Other experimental treatments may be available at other research centers.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

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. The purpose of this research study is to evaluate the safety and efficacy of duvelisib for CLL/SLL no longer responding to ibrutinib or CLL/SLL with mutations in certain genes that would eventually prevent ibrutinib from working. Duvelisib is approved by the U.S. Food and Drug Administration (FDA) to treat CLL/SLL after 2 prior therapies, but has not been specifically tested after treatment with ibrutinib.

WHAT WILL HAPPEN DURING THE STUDY?

If you decide to take part in this study, you will be asked to:

- Complete physical exam, laboratory tests, CT scan, bone marrow biopsy, and possibly lymph node biopsy and/or lymphapheresis before starting duvelisib.
- Take duvelisib twice daily and continue ibrutinib at your current dose for the first 6 months to prevent your CLL/SLL from worsening if ibrutinib is suddenly stopped. Ibrutinib will be supplied from the NIH Clinical Center Pharmacy. Continue to take duvelisib until your CLL/SLL stops responding or you develop intolerable side effects.
- Obtain laboratory tests every 2 weeks during the first 2 months to monitor the safety of duvelisib. These tests can be performed at an outside laboratory provided you share the results with us.
- Return to the NIH Clinical Center every month for follow-up during the first 6 months and every 3 months thereafter. We will perform a physical exam and laboratory tests at these visits and CT scans and procedures described below. You may be asked to come more frequently if your CLL/SLL does not respond to treatment or you develop side effects.
- Undergo a CT scan to see how your CLL/SLL is responding to treatment after 3 months, 6 months, 12 months on duvelisib, and annually thereafter.
- Undergo a bone marrow biopsy after 3 months and 6 months on duvelisib and when you achieve complete remission.

Some of your blood samples obtained during this study may be stored for the duration of the study. Your identity will be protected by using a code, such as a number, to label these samples. These blood samples may be used for the following:

- Research associated with this study.
- Future research or be given to another investigator for future research without consent. Any such research would either protect or remove any personally identifiable information about you.
- Development of medical products or processes. You will not gain financially from any products or processes that may result from this research even if your blood is used.
- DNA sequencing, including whole exome sequencing.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last as long as your CLL/SLL is responding to treatment and you do not experience intolerable side effects. Most visits will range from 4-8 hours in length and will occur every month during the first 6 months and every 3 months thereafter. If you discontinue duvelisib, then for your safety you will be asked to return approximately 30 days after your last dose of duvelisib. If you discontinue duvelisib for reasons other than disease progression or to start new anti-CLL therapy, you will also be asked to return every 6 months to monitor your CLL/SLL. After your CLL/SLL progresses or you start new anti-CLL therapy, you will be asked to return or be contacted by telephone yearly to see how you are doing.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 36 people participate in this study at the NIH Clinical Center.

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WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?**Duvelisib**

All the side effects of duvelisib are not known. The effects of duvelisib when combined with other medications or substances such as alcohol are not known and might result in serious or even life-threatening reactions. Therefore, you should always discuss the use of any drugs (over-the-counter, prescription, herbal, recreational) or substances such as alcohol, with your study doctor prior to taking duvelisib, and while you are participating in this study.

Side effects can go away while continuing to take the drug, or shortly after you stop taking the drug, but some side effects could be long-lasting, permanent, serious, life threatening, or even cause death. Everyone taking part in the study will be watched carefully for any side effects, and the drug may be stopped if intolerable or concerning side effects develop. You should talk to your study doctor about any side effects that you have while taking part in the study.

Approximately 700 subjects with blood cancers have received study treatment (either duvelisib and/or another treatment for their cancer) on studies of duvelisib. Based on available information from subjects who received duvelisib on these studies, a list of potential side effects has been identified. These potential side effects may or may not be caused by duvelisib (for example, they may be due to underlying blood cancer or other medical conditions the subjects had before the study).

Should information become available that might change your decision to participate in this study, you will be informed immediately. You can always decide whether or not to continue participating in this study. As new risks are identified, you will also be informed of these risks. You will be asked to sign a new consent form that confirms you have been made aware of the new risks and agree to continue participating in this study.

As of 19 July 2018, the side effects seen in subjects with blood cancer who have taken duvelisib alone as a single anti-cancer treatment (total daily doses range from 16 mg to 200 mg), with most subjects with blood cancer having received a total daily dose of 50 mg (25 mg 2 times a day) are listed below. Most side effects seen were mild and subjects recovered with or without holding treatment with duvelisib. However, some side effects were severe, led to hospitalization, were life-threatening, or caused death.

The most common side effects are described in the table below.

Side effects occurring in more than 25 out of 100 subjects treated with duvelisib for blood cancer were

- Infections that could be caused by a bacteria, virus, or fungus. This includes infections that affect the throat, lungs and sinuses such as the common cold or pneumonia. The most frequent infections occurred in the lungs. Infection can spread to vital organs causing the organs to not function properly (sepsis). In some cases, infections can be life-threatening and may cause death (4% fatal), such as lung infections or sepsis. In rare instances (<1%), more specific infections that would typically not occur in people with normal immunity can occur in people with decreased immune systems (such as people with cancer). Such infections may include infections with viruses such as Herpes simplex virus,

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Cytomegalovirus or Epstein-Barr virus (a virus that can cause mononucleosis otherwise known as “mono”); and infections with fungus such as Aspergillus, Candida, or Pneumocystis. Report any new or worsening signs and symptoms of infections such as fever and chills or any other sign of infection. You may require medical attention and should immediately notify your doctor for further evaluation. Your doctor may prescribe medications such as antibiotics or antivirals to help prevent some of these infections.

- Frequent loose watery stools (diarrhea) and/or inflammation of the intestines (colitis). This can be life-threatening and may cause death in rare cases (<1%). Tell your doctor right away if you have any new or worsening diarrhea, stool with mucus or blood, or if you have severe stomach-area (abdominal) pain. You may require medical attention and should immediately notify your doctor for further evaluation.
- Decrease in number of white blood cells that helps fight infection with or without fever.
- Rash which may be itchy or may cause blisters. In rare cases (<1%), you could have peeling of the skin which could be serious, life-threatening or may cause death. Tell your doctor right away if you get a new or worsening skin rash or other skin reaction including painful sores or ulcers on your skin, lips, or in your mouth, severe rash with blisters or peeling skin, rash with itching or rash with fever.
- Feeling tired or weak.
- Fever.
- Cough.
- Feeling sick to your stomach

Side effects occurring in more than 10 but less than 25 out of 100 subjects treated with duvelisib for blood cancer were:

- Abnormally high level of enzymes produced by the liver meaning that it could affect how your liver functions. Tell your doctor right away if you get any symptoms of liver problems, including yellowing of your skin or the white part of your eyes (jaundice), pain in the stomach-area (abdominal) region, bruising or bleeding more easily than normal.
- Pain in your muscles and/or joints.
- Decrease in red blood cells which can cause tiredness and shortness of breath and decrease in cells in the blood that help the blood to clot.
- Swelling which may be in a specific location or may be more generalized.
- Decreased appetite
- Sores in your digestive tract (nose, mouth, stomach, etc.) which can lead to not wanting to eat.
- Throwing up or vomiting
- Shortness of breath.
- Headache.
- Difficulty having a bowel movement or constipation.
- Abdominal pain
- Decrease in potassium in your blood which can cause muscle weakness or cramps, or changes in heart rhythms.

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In addition, a small number of subjects experienced severe inflammation of the lungs which can be serious and can lead to death in rare cases (<1%). Tell your doctor right away if you get new or worsening cough or difficulty breathing. Your doctor may do tests to check your lungs if you have breathing problems during treatment. Your doctor may treat you with a steroid medicine if you develop inflammation of the lungs that is not due to an infection.

If you have any new and concerning systemic symptoms (e.g. fevers, rigors, severe fatigue), respiratory symptoms (e.g. shortness of breath, persistent cough, chest pain), or gastrointestinal symptoms (e.g. diarrhea or blood in your stool), you should immediately notify your doctor for further evaluation.

Additional Potential Effects While on Treatment with duvelisib

Exposure to Sun: The effect of duvelisib on the skin, especially when in direct sunlight or with artificial UV light (e.g. tanning booths), is not known. As a general precaution, it is advised to use appropriate protective measures (e.g. long sleeve shirts and pants, hat, umbrella) to minimize exposure to direct sunlight during the treatment period and for at least 30 days after the last dose of duvelisib.

Vaccinations: Tell your study doctor if you have had a recent vaccination or are scheduled to receive vaccinations. You should not receive certain vaccines after starting duvelisib. Vaccinations while on duvelisib may not work or could result in infection. Tell your doctor if anyone in your household is scheduled to receive a vaccination.

Drug-drug interactions: If you start any new medications (prescriptions, herbal and/or over the counter), inform your doctor. Drug-drug interactions can decrease how well your medications work, may increase minor or serious unexpected side effects, or even increase the blood level and possible toxicity of a certain drug.

Ibrutinib

To be eligible for this study, you must be currently taking ibrutinib. Ibrutinib is an U.S. FDA approved for treatment of CLL. The table below lists the most common side effects seen in patients who have taken ibrutinib.

Most Common ($\geq 20\%$)	Very Common ($\geq 10\%$)	Less Common ($\geq 1\%$)
<ul style="list-style-type: none"> • Increase in frequency of loose or watery stools (diarrhea) • Bruises • Muscle and bone/joint pain (musculoskeletal pain) • Nausea • Rash 	<ul style="list-style-type: none"> • Swelling of the hands or feet (peripheral edema) • Sinus infection (sinusitis) • Common cold (upper respiratory infection) • Fever • Constipation • Joint aches (arthralgia) 	<ul style="list-style-type: none"> • Dizziness • Urinary tract infection • Low white blood cells with fever (febrile neutropenia) • Abnormal heart rhythm (atrial fibrillation) • Blurry vision

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<ul style="list-style-type: none"> • Low white blood cell count, cells that help fight infection (neutropenia) 	<ul style="list-style-type: none"> • Mouth sores (stomatitis) • Headache • Pneumonia • Vomiting • Muscle spasms • Severe infection throughout the body • Low platelet count, cells that help blood to clot (thrombocytopenia) • High blood pressure (hypertension) • Skin infection 	<ul style="list-style-type: none"> • Increase in white blood cell counts (leukocytosis) • Breaking of the nails (onychoclasia) • Inflammation of the lungs that could lead to permanent damage (interstitial lung disease) • Nose bleed (epistaxis) • Non-melanoma skin cancer (basal cell and squamous cell carcinoma) • Severe infection throughout the body (sepsis) • Skin redness (erythema) • Increased level of uric acid in the blood (hyperuricemia) • Small purple or red spots caused by bleeding under the skin (petechiae) • Increase in lymphocyte count (lymphocytosis)
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Blood Sampling

Risks associated with drawing blood or needle sticks include pain, bruising, bleeding, light-headedness, inflammation, temporary redness of the skin at the place the needle is put into your arm, fainting, and, on rare occasions, infection and/or local clot formation.

Bone Marrow Biopsy

A local anesthetic will be injected at the site of bone marrow biopsy. There may be a stinging or burning sensation from the injection. The biopsy needle will be placed through the skin and into the bone and may produce a brief, dull pain. As the bone marrow liquid is withdrawn from the bone, there may be a brief, sharp pain. Since the interior of the bone cannot be anesthetized, this procedure may cause some discomfort, however not all patients experience these symptoms. In some cases, the doctor may prescribe some medication used as conscious sedation. This is given to you to help you relax if the doctor feels it is necessary.

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Some risks associated with this procedure include persistent bleeding and infection, pain after the procedure at the site where the bone marrow biopsy is done, and sometimes very infrequently a nerve may be injured during the procedure causing pain.

Lymph Node Biopsy (Optional)

There are several ways to do a lymph node biopsy.

In a fine-needle or core needle aspiration biopsy, a thin needle is used to remove cells from the lymph node. Patients will feel only a quick sting from the local anesthesia used to numb the skin and may feel some pressure from the biopsy needle. After a fine-needle aspiration biopsy or core needle biopsy, the site may be tender for 2 to 3 days.

In an open biopsy, the lymph node is removed through a cut in the skin. This can be done under local anesthesia. After the open biopsy, the biopsy site may feel tender, firm, swollen, and/or bruised. Subjects may be advised to not do any heavy lifting or other activities that stretch or pull the muscles around the area.

As patients are at risk of infection at the biopsy site, we will ask you to report any swelling, redness or discharge to the research team so that appropriate antibiotics can be started if necessary.

I give my permission for my lymph node biopsy:

_____ Yes _____ No

Initials Initials

CT Scans

Before the CT scan a contrast dye (iodine dye) may be injected into your vein. These injections may cause a slight discomfort, bruising, swelling and sometimes an allergic reaction, although this is rare. If an allergic reaction occurs, it can range from being mild (itching, rash) to severe (difficulty breathing, shock, or rarely, death). In addition, contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies, kidney problems, or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan.

Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when you are inside the scanner, or by lying in one position for a long time. The contrast material may make you feel discomfort when it is injected/given by mouth. You may feel warm and flushed and get a metallic taste in your mouth. Rarely, the contrast material may cause nausea, vomiting, or a headache.

Lymphapheresis (Optional)

Blood will be taken from your body (from an IV in your arm) and sent through a machine to remove white blood cells. Blood without white blood cells will be returned to you (through an IV in your other arm).

If you choose to have lymphapheresis, you might feel lightheadedness or have bleeding from the sites where blood is taken or returned. Low blood pressure and muscle cramps can occur during the procedure. If you feel uncomfortable, you should tell the study team. There is also the chance for infection after the procedure.

I give my permission for my blood to be taken for lymphapheresis:

_____ Yes _____ No

Initials Initials

What are the risks related to pregnancy?

Duvelisib has not been tested to determine whether it may have an effect on pregnancy or a developing baby.

All patients enrolled in the study and their partners should agree to take effective measures in order to prevent a pregnancy from the screening visit up to 30 days after the last dose of duvelisib. You must also agree not to donate sperm during this period.

If you are pregnant or plan to become pregnant, you will not be allowed to participate in this study because of possible harm to you or your baby. Females who are capable of bearing children will be required to take a pregnancy test prior to entry into this study and during the study. If at any time during the study and up to 30 days after you take the last dose of duvelisib you suspect that you have become pregnant, please notify the study doctor immediately.

If you become pregnant, you will be permanently taken off study drug(s), but we will continue to follow you at regular intervals.

If you are a male study participant, you should agree to protect your partner from becoming pregnant before and during the study and for up to 30 days after your last dose of duvelisib. If your partner becomes pregnant while you are on study and for up to 30 days after discontinuing the study, you must immediately notify the research study staff. We can provide counseling about preventing pregnancy for either male or female study participants.

To participate in this study, you should agree to use an effective method of birth control to prevent pregnancy. Acceptable methods to prevent pregnancy during participation in this study and for 30 days after the last dose of duvelisib are:

- Total abstinence (no sexual intercourse).
- Surgical sterilization including tubal ligation (tubes tied) or hysterectomy (removal of uterus or womb) in women or a vasectomy in men.
- Oral contraceptives (birth control pills), intrauterine devices (IUD), implantable or injectable contraceptives in combination with barrier methods (such as a condom or diaphragm) used with a spermicide.
- Barrier methods (such as a condom or diaphragm) used with a spermicide.

The contraception methods described above may not protect against HIV infection (AIDS) and other sexually transmitted diseases. If you need more information about this, please ask your study doctor.

You should not nurse (breastfeed) a baby while on this study because duvelisib may enter breast milk and possibly harm your child.

What are the risks of radiation from being in the study?

You may have up to 4 CT scans during the first year of the study, one of which you may have already had as part of your screening visit. The CT scan done after completion of 3 month and 6 months of duvelisib is medically indicated. The other CT scans (at the completion of one year on duvelisib and once a year for as long as you remain on treatment), will be done for research purposes if not required for your medical care. The amount of radiation you will receive in this study is 1.3 rem per year for annual research scans, which is below the guideline of 5 rem (or 0.5 rem in children) per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. Although it is important for this research, you may choose not to undergo the CT scans that are scheduled for research purposes. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer. Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body. If you are pregnant you will not be permitted to participate in this research study. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You will not benefit from being in this study.

However, the potential benefit to you might be that duvelisib will help treat your CLL/SLL. If you decide to participate in this study, your health will be monitored very closely which may provide a benefit to you.

In the future, other people might benefit from this study because you will give doctors more information about how well duvelisib works. It may help doctors understand your condition better and may help future patients with CLL/SLL.

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

In the future, other people might benefit from this study because we will have better understanding how this medication can help other patients.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could choose to be treated by your home health care provider. Venetoclax (Venclexta®) is a Bcl-2 inhibitor approved for previously treated CLL/SLL. Idelalisib (Zydelig®), a PI3Kδ inhibitor, combined with rituximab (Rituxan®), a monoclonal antibody, and duvelisib (Copiktra®) is approved for CLL/SLL after 2 prior therapies. If you received ibrutinib as the first treatment for your CLL/SLL, chemotherapy combined with monoclonal antibody is also an option. Other experimental treatments may be available at other research centers.

DISCUSSION OF FINDINGS

New information about the study

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

Return of research results

Clinically relevant research results will not be shared with you.

EARLY WITHDRAWAL FROM THE STUDY

Your participation is entirely voluntary. You may choose to stop at any time. If you stop because of side effects, you might be asked to return for additional tests until the side effects resolve. New information regarding safety and effectiveness of duvelisib may become available. Following discussion of that new information with the research team:

- You may decide to discontinue participation
- You may decide to continue in the study, if so we will ask you to sign an updated consent form
- The research team may decide it is not in your best interest to continue in the study

The principal investigator of this study (Clare Sun, MD), the Institutional Review Board (IRB), and Verastem, Inc. may stop this study at any time, for any reason, without your consent. For safety reasons, the Data Safety Monitoring Board may also recommend stopping this study without your consent.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide

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additional information that will be helpful in understanding Lymphoma, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

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

_____ Yes _____ No
Initials Initials

Will your specimens or data be shared for use in other research studies?

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

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

_____ Yes _____ No
Initials Initials

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

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

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

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH until they are no longer of a scientific value, at which time they will be destroyed.

Risks of storage and sharing of specimens and data

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

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

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

You will not receive compensation for participation in this study.

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

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

This study will offer reimbursement for, or payment of, travel, lodging or meals according to NIH and NHLBI policies and guidelines.

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.

CONFLICT OF INTEREST (COI)

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

The NIH and the research team for this study are using duvelisib developed by Verastem, Inc. through a joint study with your study team and the company. The company also provides financial support for this study.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

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

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor (NHLBI Division of Intramural Research)
- Qualified representatives from Verastem, Inc., the pharmaceutical company who produces duvelisib.

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

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

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

Certificate of Confidentiality

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

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

The Certificate does not protect your information when it:

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

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

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

Privacy Act

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

POLICY REGARDING RESEARCH-RELATED INJURIES

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

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Clare Sun, clare.sun@nih.gov, 301-402-1806. *Other researchers you may call are:* Pia Nierman, pia.nierman@nih.gov, 301-827-1094. 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

Parent/Guardian of a Minor Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I give permission for my child to take part in this study.

Signature of Parent/Guardian

Print Name of Parent/Guardian

Date

Signature of Parent/Guardian (*as applicable*)

Print Name of Parent/Guardian

Date

Assent: (*Use this section only when this process is approved by an IRB for older minors. Do not use if an IRB requires a separate assent form for this population.*)

I have had this study explained to me in a way that I understand, I have been given the opportunity to discuss it, and I have had the chance to ask questions. I agree to take part in this study.

Assent of Minor: (*as applicable*)

Signature of Minor

Print Name of Minor

Date

Investigator:

Signature of Investigator

Print Name of Investigator

Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process with a non-English speaking subject and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*

Print Name of Witness

Date

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

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

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