RESEARCH CONSENT FORM

H: 34138: IDELALISIB FOR IGM-ASSOCIATED AL AMYLOIDOSIS

Background

Before agreeing to participate in this study, it is important that the following explanation of the research study be read and understood. This form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes alternative procedures available and the right to withdraw from the study at any time. It is important to understand that no guarantee or assurance can be made as to the results. It is also understood that refusal to participate in this study will not influence your rights to receive standard treatment or other therapies.

You are being asked to take part in this research study because you have a form of AL amyloidosis, which has unique type of diseased cell (called an IgM antibody). The diseased cells in most forms of AL amyloidosis are similar to a cancer called multiple myeloma. Standard treatment options for patients with AL amyloidosis include high dose melphalan with stem cell transplant or the drugs revlimid, bortezomib, cytoxan and dexamethasone, alone or in combination.

However, in this small subset of AL Amyloidosis patients, the cells are typically related to a different type of cancer, called lymphoplasmacytic lymphoma or Waldenstrom's macroglobulinemia. This type of cells may respond better to different medications than those typically used with most types of AL amyloidosis, such as rituximab and idelalisib.

Participants in this clinical trial will receive the drug idelalisib. Idelalisib is a drug, taken by mouth, which has been shown to be effective against blood cancers similar to your disease. Idelalisib is an investigational drug, which means it has not been approved by the U S Food and Drug Administration (FDA) for AL Amyloidosis.

Your treating doctor is also an investigator of this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

Purpose

The purpose of this study is to evaluate the safety and effectiveness of using the drug idelalisib in patients with IgM-associated AL Amyloidosis.

Duration

The duration of your participation in this study will be for as long as your disease does not get worse and your side effects are manageable. This could be for several months to a year or more. There will be about 18 participants involved in this study. Your disease status will be followed until disease progression or you begin another treatment.

Procedures

The research will take place at the following location(s): Boston University Medical Center.

If you agree to participate in this study, you will begin taking Idelalisib pills in 28-day cycles as described below:

Idelalisib: You will take idelalisib by mouth twice each day for as long as your disease does not get worse and your side effects are manageable. Idelalisib should be taken at the same time each day. If a dose is missed, it can be taken up to 6 hours after the scheduled time with a return to the normal schedule the following day. If it has been over 6 hours, the dose should not be taken (skip that dose) and you should take the next dose at the scheduled time the next day. If the pills are vomited, do not take a replacement. Please let your study doctor know if you vomit while you are participating in the clinical trial. You will be asked to document on a pill diary the day and time that each dose is taken. Please bring the pill diary with you to each study visit.

You will continue to receive idelalisib until such time that your disease gets worse, you experience unacceptable side effects or you wish to discontinue therapy. You will be asked to return any unused study drug and empty bottles to the clinic at each visit.

Bactrim DS: Idelalisib can increase the risk of pneumonia. Therefore, you will also need to take Bactrim DS, which is an antibiotic, to help prevent pneumonia as long as you are taking idelalisib on this study. It is important to remember to take the antibiotic as instructed.

While participating in this study, you should avoid eating Seville oranges, star fruit and grapefruit or drinking grapefruit juice, green tea or foods/supplements containing green tea or extract as these may interfere with the study drug. In addition, please be sure to tell your study doctor about any medication you may be taking including over-the-counter medications, vitamins, herbal, homeopathic or holistic medications or treatments. This is important because a possible interaction with some medications, vitamins, and remedies may cause serious side effects, and/or may still be unknown.

Before you begin study treatment, you will have the following tests and exams. They are standard for your disease and may not need to be repeated for the study.

- History & Physical Exam
- Quality of Life Questionnaire (SF-36)
- Blood tests
- Hepatitis and HIV blood test, and for women of childbearing potential a pregnancy test
- Urine tests, including a 24 our collection of your urine
- Bone marrow biopsy
- Fat aspirate (if not previously done)
- Chest x-ray

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- EKG (to monitor the electrical activity of the heart)
- Echocardiogram (to test the heart function)
- Pulmonary Function tests (to measure the function of your lungs)

Every 2 weeks for the first 6 months after starting Idelalisib:

- Blood tests. Your liver tests and blood counts must be closely monitored on this medication.

Monthly while taking Idelalisib:

- Blood tests to test for viral and fungal infections.

One and 2 months after starting Idelalisib

- Quality of Life Questionnaire (SF-36)
- Blood tests

Every 3 months while on Idelalisib

- History & Physical Exam
- Quality of Life Questionnaire (SF-36)
- Blood tests
- Urine tests

Every 6 months while on Idelalisib

- Echocardiogram
- Urine tests, including a 24 our collection of your urine

Within 30 days after stopping Idelalisib

- History & Physical Exam
- Blood tests

Subjects who have responded to the study drug, but have discontinued treatment for reasons other than disease progression, will continue to be evaluated every 6 months until disease progression, starting a new line of therapy, or withdrawing consent:

- History & Physical Exam
- Blood tests
- Urine tests
- Echocardiogram

Risks/ Discomforts

There is always a risk involved in taking any drugs, but you will be carefully monitored for any problems and you are encouraged to report anything that is bothering you. There may be risks or side effects of the study drug that are unknown or cannot be predicted at this time. You should

not hesitate to report anything that upsets you or may be troubling you to your Study Doctor, even if you do not think it is connected to taking the study drug. If you have any questions you should contact the Study Doctor or his/her staff.

Risks of Idelalisib:
Patients in clinical trials for other diseases taking idelalisib in combination with chemotherapy were found to have a higher chance of serious side effects and death than patients not receiving idelalisib. This increased risk was only seen in patients who had never received chemotherapy before. Most of the incidents of death were attributed to serious infections that may be more likely in patients receiving idelalisib.

The following risks were experienced in more than 10% of people taking idelalisib:
- Decreased white blood cell count is common and can increase risk of infection. In some cases, these infections have been fatal
- Decreased platelet count, which can increase risk of bleeding
- Trouble sleeping
- Fatigue
- Headache
- Skin reactions, which could be severe
- Night sweats
- Diarrhea from swelling of the colon, which can result in a tear in the wall of the intestine which may cause abdominal pain, chills, fever, nausea or vomiting. In some cases this has been fatal.
- Nausea
- Vomiting
- Abdominal pain
- Decreased appetite
- Liver problems (which can be serious, and in rare cases can result in death)
- Weakness
- Cough
- Pneumonia
- Difficulty breathing
- Infection
- Fever
- Joint pain

The following risks were experienced in 1-10% of people taking idelalisib:
- Swelling in the arms and legs
- Swelling of the lung tissue, which may cause cough and shortness of breath, and fatigue. In some cases this reaction has been fatal

- Tear in the wall of the intestine which may cause abdominal pain, chills, fever, nausea or vomiting, and in rare cases may lead to death
- Allergic reaction, which can cause shortness of breath

Risks of Bactrim DS:
The following side effects and risks have been seen in patients taking Bactrim DS.

- Decreased white blood cells, which can increase your risk for infections
- Decreased red blood cells, which can cause you to feel tired and weak.
- Decreased platelets, which can increase your risk of bleeding (in rare cases can be severe and could lead to death)
- Allergic reactions
- Serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), which can result in death and can occur without warning
- Swelling of the pancreas
- Inflammation of the liver
- Mouth sores
- Nausea
- Vomiting
- Diarrhea (which in rare cases can be serious)
- Abdominal pain
- Decreased appetite
- Trouble sleeping
- Kidney failure
- Liver failure
- Problems urinating
- Abnormal balance of minerals in the body
- Convulsions
- Abnormal muscle coordination
- Headache
- Dizziness
- Hallucinations
- Depression
- Cough
- Shortness of breath
- fever
- Fluid around the lining of the lung
- Joint pain
- Muscle pain

Your health care team may give you medicines to help lessen or treat side effects. Many side effects go away soon after you stop taking study drug. In some cases, side effects can be serious, long-lasting or may never go away. You should talk to your study doctor about any side effects that you have while taking part in the study.

Reproductive risks:
The drugs used in this study can affect an unborn baby. Therefore, if you are pregnant or nursing a child, you cannot take part in this study (women of child bearing potential will be asked to take a urine test to see if they are pregnant before starting in this study). If you are a sexually active male or female, you must prevent the possibility of becoming pregnant or fathering a child while on this study. You must use birth control while you are participating in this study and for one month afterward. The only birth control methods that work well enough to be safe while you are on this study are oral contraceptives ("the pill"), intrauterine devices (IUDs), contraceptive implants under the skin, or contraceptive injections, diaphragms with spermicide and condoms with foam. You should not participate in this study if you practice heterosexual sex and cannot use one of these birth control methods to prevent the possibility of becoming pregnant or fathering a child while on this study.

Blood samples and/or injections may result in fainting, pain, bruising, swelling or bleeding at the site where the blood is drawn. All appropriate measures will be taken to avoid these occurrences.

There is always a risk of release of information from your health records. We will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small.

There may be unknown risks/discomforts involved. Study staff will update you in a timely way on any new information that may affect your health, welfare, or decision to stay in this study

Other Risks
Please let your Study Doctor know all of your present and past diseases and allergies and any medication you may be taking including over-the-counter medications, vitamins, herbal, homeopathic or holistic medications or treatments. This is important because a possible interaction with some medications, vitamins, and remedies may cause serious side effects, and/or may still be unknown.

What are my responsibilities?
- Keep your study appointments. If you cannot keep an appointment, contact your study doctor or study staff to reschedule as soon as you know that you will miss the appointment.
- Tell your study doctor or study staff about any medications you are taking.
- Tell your study doctor or study staff about any side effects, doctors' visits, or hospitalization that you may have whether or not you think they are related to the study therapy.
- Tell your study doctor if you have been in a research study in the last 30 days or are in

another research study now. While participating in this research study, you should not take part in any other research project without approval from your study doctor. This is to protect you from possible injury arising from such things as extra drawing of blood samples, possible reaction between research drugs, or other hazards.

Benefits

Taking part in this study may or may not make your health better. Using idelalisib may be more useful against IgM-associated AL amyloidosis compared to the usual treatment, although there is no proof of this yet. There may be no benefit.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study:

- As with any treatment recommendation, you can get a second opinion if you wish.
- You can get treatment for your disease without being on this study. All of the treatment on this study may be available at this center or at other locations;
- You may receive other types of chemotherapy or steroids (alone or in combination) alone or in combination;
- You may choose no therapy at this time with care to help you feel more comfortable

Confidentiality

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

- the Institutional Review Board of Boston Medical Center and Boston University Medical Center (BMC/BUMC IRB), a group of people who review the research study to protect your rights;
- Government agencies, including the NCI or its authorized representatives, the FDA, the Office for Human Research Protections (OHRP). These agencies may review the research to see that it is being done safely and correctly.
- Gilead Sciences, Inc., the manufacturer of Idelalisib, who is providing support for this research study, or their agents or designees

Information from this study and from your medical record may be used for research purposes and may be published; however, your name will not be on the publications.

Costs

The drug idelalisib will be provided free of charge to you for the purposes of this study by the drug manufacturer, Gilead Sciences, Inc. The cost of Bactrim DS is not covered by the study and must be paid by you and/or your insurance company, including any applicable co-payments. You should review with the study team what the costs to you will be. Bactrim DS is necessary in

this study, but you may not need to take it if you do not participate in this study. You are free to decline participation, or withdraw from the study if you do not want to pay the cost of Bactrim DS. You or your insurance company will be billed for all other costs of treatment and exams related to this study.

You will not be paid to participate in this research study.

Subject's Rights

By consenting to participate in this study you do not waive any of your legal rights. Giving consent means that you have heard or read the information about this study and that you agree to participate. You will be given a copy of this form to keep.

If at any time you withdraw from this study you will not suffer any penalty or lose any benefits to which you are entitled.
You may obtain further information about your rights as a research subject by calling the Office of the Institutional Review Board of Boston University Medical Center at 617-638-7207.

The investigator or a member of the research team will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury while participating in this research, contact Mark Sloan, MD at 617-638-8265 during the day and the hematologist on call via the hospital's page operator at 617-638-7243 after hours.

Compensation for Research Related Injury

If you think that you have been injured by being in this study, please let the investigator know right away. You can get treatment for the injury at Boston Medical Center. You and your insurance company will be billed for this treatment. Boston Medical Center does not offer a program to provide compensation for the cost of care for research related injury or other expenses such as lost wages, disability, pain, or discomfort. You will be sent a bill for the medical care you receive for research injury if your medical insurance does not pay for your medical care. You are not giving up any of your legal rights by signing this form.

Right to Refuse or Withdraw

Taking part in this study is voluntary. You have the right to refuse to take part in this study. If you decide to be in the study and then change your mind, you can withdraw from the research. Your participation is completely up to you. Your decision will not affect your being able to get health care at this institution or payment for your health care. It will not affect your enrollment in any health plan or benefits you can get. If you choose to take part, you have the right to stop at any time. If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them as soon as possible. The investigator may decide to discontinue your participation without your permission because he/she may decide that staying in the study will be bad for you, or the sponsor may stop the study.

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Protection of Subject Health Information

You have the right to know who will get your health information and why they will get it. Signing this form gives the researchers your permission to obtain, use, and share information about you for this study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care. If you choose to be in this research study, we will use and share health information about you as explained below.

HEALTH INFORMATION ABOUT YOU THAT MIGHT BE USED OR GIVEN OUT DURING THIS RESEARCH:

- Information from your hospital or office health records at BUMC/BMC or elsewhere when this information is related to the conduct and oversight of the research study.
- If health information is needed from your doctors or hospitals outside of BUMC/BMC, you will be asked to give permission for these records to be sent to the researcher.
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

WHY HEALTH INFORMATION ABOUT YOU MIGHT BE USED OR GIVEN OUT TO OTHERS

- To do the research described in this consent form
- To make sure we do the research according to certain standard set by ethics, law, and quality groups

PEOPLE AND GROUPS THAT MAY USE OR GIVE OUT YOUR HEALTH INFORMATION:

PEOPLE OR GROUPS WITHIN BMC

- Researchers involved in this research study
- The BUMC/BMC Institutional Review Board that oversees this research
- Non-research staff within Boston Medical Center who need this information to do their jobs [such as for treatment, payment (billing), carrying out research team orders for hospital and health care services related to research study participation (e.g., laboratory tests, diagnostic procedures) or health care operations.

PEOPLE OR GROUPS OUTSIDE BMC

- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers.
- Federal and state agencies if they are required by law or involved in research oversight. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, the Massachusetts

Department of Public Health or other U.S. or foreign government bodies if required by law or necessary for oversight purposes.

- Organizations that make sure healthcare standards are met
- The sponsor(s) of the research study, and people or groups it hires to help them do the research
- Other researchers that are part of this research study
- A group that oversees study information and safety.
- Gilead Sciences, Inc, the manufacturers of idelalisib

Some people or groups who get your health information might not have to follow the same privacy rules that we follow. We share your health information only when we must. We ask anyone who gets it from us to protect your privacy. However, once the information leaves BU or BMC, we cannot promise that it will be kept private.

In most cases any health data that is being given out to others is identified by a unique study number and not with your name. So, although in some cases it is possible to link your name to the study data, this is not usually done.

TIME PERIOD FOR USING OR GIVING OUT YOUR HEALTH INFORMATION
The use of your health information has no specific expiration date.

YOUR PRIVACY RIGHTS
You have the right not to sign this form that allows us to use and give out your health information for research. If you don't sign this form, you can't be in the research. This is because we need to use the health information to do the research.

You have the right to withdraw your permission to use or share your health information in this research study. If you want to withdraw your permission, you must write a letter to the researchers in charge of this research study.

If you withdraw your permission, you will not be able to take back information that has already been used or shared with others. This includes information used or shared to do the research study or to be sure the research is safe and of high quality.

If you withdraw your permission, you cannot continue to be in the study.

You have the right to see and get a copy of your health information that is used or shared for research. However, in some situations, you may not be able to get this until after the research is finished. To ask for this information, please contact the person in charge of this research study.

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IF RESEARCH RESULTS ARE PUBLISHED OR USED TO TEACH OTHERS
The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information will not be used for these purposes without your specific permission.

If Research Results Are Published Or Used To Teach Others
The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information will not be used for these purposes without your specific permission.

Where can I get more information?
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.

Consent
Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

_____/_____
Subject (Signature and Printed Name) **Date**

_____/_____
Investigator or Designee (Signature and Printed Name) **Date**