THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase II Study of Acalabrutinib in Ibrutinib-Intolerant Mantle Cell Lymphoma
2019-0421

Subtitle: Version 13 – 4.25.2023

Study Chair: Preetesh Jain

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if acalabrutinib can help to control mantle cell lymphoma (MCL) in patients that cannot tolerate ibrutinib. The safety of this drug combination will also be studied.

This is an investigational study. Acalabrutinib is FDA approved and commercially available for the treatment of MCL. The study doctor can describe how the drug is designed to work.

The study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects that may be severe or fatal.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may continue the drug as long as the disease does not get worse, you do not have intolerable side effects, or your doctor does not think you should continue the drug.

Acalabrutinib and will be provided to you at no cost while you are receiving treatment on this study.

You may choose not to take part in this study. Instead of taking part in the study, you may choose to receive standard chemoimmunotherapy. The doctor will discuss with you the risks and benefits of these alternative treatments. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Visit

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- You will have an EKG and an echocardiogram (ECHO) scan to check your heart function. If the study doctor thinks it is needed, you may also have a MUGA scan.
- You will have a chest x-ray to look for any infections or other possible problems in the chest area and to check your heart function and the status of the disease.
- Blood (about 4 teaspoons) for routine tests, to check the status of the disease, and for research antibody testing. Antibodies are created by the immune system and may attack foreign cells or substances, such as the study drug.
- Urine will be collected for routine tests.
- If you can become pregnant, part of the above blood or urine sample will also be used for pregnancy tests.
- You will have a bone marrow biopsy and/or aspiration to check the status of the disease. To collect a bone marrow aspirate and biopsy, an area of the hip is numbed with anesthetic, and a small amount of bone marrow and bone is withdrawn through a large needle.
- You will have a PET/CT scan of your entire body to check the status of the disease.
- If the doctor thinks it is needed, you will have a colonoscopy or endoscopy to check the status of the disease. The study doctor can describe these procedures in more detail, if needed.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Up to 30 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each cycle is 28 days. You will take acalabrutinib by mouth 2 times each day while you are on study (about 12 hours apart each time).

Tablets should be swallowed whole with about a cup (8 ounces) of water. They may be taken with or without food. You should not break, open, or chew tablets. If a dose of acalabrutinib is missed by more than 3 hours, it should be skipped, and the next dose should be taken at its regularly scheduled time. You should not take extra tablets to make up the missed dose.

You will no longer be able to take the drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over once you have completed your long-term follow-up.

Study Visits

On **Day 1 of each cycle**

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, research antibody testing, and to check the status of the disease.
- Urine will be collected for routine and research antibody testing.
- If you can become pregnant, part of the above blood or urine sample will also be used for pregnancy tests.

Every 3 cycles:

- You will have a bone marrow biopsy and/or aspiration to check the status of the disease.
- You will have a PET/CT scan of your entire body to check the status of the disease.

If you had a colonoscopy or endoscopy at screening, this will be repeated whenever the study doctor thinks it is needed to check the status of the disease.

End-of-Study Drug Visit

After you finish taking the study drugs:

- You will have a physical exam.
- Blood (about 4 teaspoons) for routine tests, to check the status of the disease, and for research antibody testing.
- Urine will be collected for routine tests.
- If you can become pregnant, the above blood or urine sample will also be used for a pregnancy test.
- You will have PET/CT scan of your entire body to check the status of the disease.
- If the study doctor thinks it is needed, you will have a bone marrow biopsy and/or aspiration to check the status of the disease.
- If you had a colonoscopy or endoscopy at screening, this will be repeated

Follow-Up Visits

Progression-free Survival (PFS) Follow-Up
If you stop taking the drug at any time for reasons other than the disease getting worse, you will have follow-up clinic visits to check on how you are doing. These follow-up visits will occur as per the following schedule, unless the disease gets worse:

- Every 4 months (+/-1 month) during Year 1-2 after your last dose
- Every 6 months (+/- 2 months) during Year 2-4
- Every year (+/-3 months) after that until the end of the study

At these visits, you will have blood (about 4 teaspoons) drawn for routine tests and imaging scans (such as CT scans or PET/CT scans) to check the status of the disease.

Overall Survival Follow-up
After your end-of-study drug visit, the study team will call you to check on how you are doing. These follow-up calls will take about 2-3 minutes each time and will occur on the following schedule:

- Every 4 months (+/- 1 month) during Year 1-2 after your last dose
- Every 6 months (+/- 2 months) during Year 2-4
- Every year (+/- 3 months) after that until the end of the study

Additional Information

While you are on study, do not have any foods or drinks containing grapefruit, pomegranate, or Seville (sour) orange juice.

Ask the study doctor before taking any new drugs during the study. This includes over-the-counter drugs and herbal and natural remedies. Your study doctor will review all of the drugs you are taking and let you know if they can be taken during the study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Acalabrutinib Side Effects

Common (occurring in more than 20% of patients)

• headache • fatigue • skin rash	• diarrhea • bruising	• nausea • muscle pain

Occasional (occurring in 3-20% of patients)

• irregular heartbeat (possible fainting, chest pain, and/or difficulty breathing)	• vomiting • constipation • abdominal pain • bleeding • low blood cell count (red, white, platelets)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • severe infection • nosebleed

Acalabrutinib can cause low blood cell counts (red, white and/or platelets):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.

Acalabrutinib may cause you to develop another type of cancer.

Rare but serious (occurring in fewer than 3% of patients)

• reactivation of hepatitis B infection (liver damage)	• severe bleeding (possibly in the digestive system and/or brain)

If you are taking blood thinners (such as Warfarin), this may increase your risk of bleeding.

Acalabrutinib may cause progressive multifocal leukoencephalopathy (PML). PML is brain damage that is likely to result in paralysis and/or coma, which may be permanent. PML can also lead to death.

Based on side effects seen in similar drugs, acalabrutinib also may cause life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure).

<u>Other Risks</u>

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is

drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

EKGs/ECHOs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

PET/CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

X-rays send a small amount of radiation though the body. All radiation adds up over a lifetime and may increase the risk of a new cancer forming.

Having **bone marrow biopsies/aspirates** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Having a **colonoscopy/endoscopy** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the collection site of the collections. An allergic reaction to the anesthetic may occur. A scar may form at the collection site. It may cause bleeding and/or puncture at the site of the collection. It may also cause sore throat, bloating, and abdominal pain.

Although every effort will be made to keep **study data** safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality.** All study data will be stored in password-protected computers and/or locked file cabinets during the study and will continue to be stored securely after the study. Only authorized people who are working on this study will have access to study data.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study.

You must use highly effective methods of birth control during the study if you are sexually active.

Highly effective methods of birth control include intrauterine device (IUD), sterilization of you or your partner, birth control implants, pills, injections, patches, or rings, or male or female condom (not to be used together). If you can become pregnant and are sexually active, you must use highly effective methods of birth control during treatment and for one week after the last dose of acalabrutinib.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. Male participants should use barrier contraception even if they have had a successful vasectomy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away. The sponsor will ask for information about the pregnancy.

Getting pregnant may result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or AstraZeneca Pharmaceuticals for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Preetesh Jain, at 713-745-8432) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. The doctor will ask you to have an end-of-study visit as described above to make sure you are stopping the study drug safely. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   The study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, AstraZeneca Pharmaceuticals, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

   Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: AstraZeneca Pharmaceuticals.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and AstraZeneca Pharmaceuticals and/or shared with other researchers and/or institutions for use in future research.

Samples
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by AstraZeneca Pharmaceuticals may be used in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research
Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Conflict of Interest
Dr. Michael Wang (Study Co-Chair) has received compensation from AstraZeneca as a Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

Outside Care
Part of your care may be provided outside of MD Anderson by your home doctor(s).

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - AstraZeneca Pharmaceuticals LP and its Affiliates located around the world, as well as companies who work for AstraZeneca Pharmaceuticals who may also be located around the world
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line.)