RESEARCH SUBJECT INFORMATION CONSENT FORM

TITLE:	A Phase 1, Open-label, Study of Voruciclib in Subjects with Relapsed and/or Refractory B-Cell Malignancies or Acute Myeloid Leukemia After Failure of Prior Standard Therapies and Voruciclib in Combination with Venetoclax in Subjects with Relapsed and/or Refractory Acute Myeloid Leukemia
PROTOCOL NO.:	ME-522-001
SPONSOR:	MEI Pharma, Inc.
INVESTIGATOR:	Name Address City, State, Zip Country
STUDY-RELATED PHONE NUMBER(S):	Name Phone number(s) (24-hour phone number required)

You are being asked to participate in a clinical research study in patients with acute myeloid leukemia (AML) that have relapsed (come back) or are refractory (did not respond to previous treatment).

This informed consent form (ICF) describes what is involved in this research study. It explains the tests, treatments, and other details of what will happen to you if you decide to participate. Please read this information carefully. Ask your study doctor or a member of the research team to explain anything you do not understand or want to know more about. Before deciding whether or not to take part, you may want to discuss this with a relative, friend or your local doctor.

Your participation in this research study is voluntary. If you do not want to take part, you do not have to, and it will not affect the care you receive in any way.

If you decide to participate, you will need to sign and date this ICF. Your signature means that you:

- Understand what you have read

- Agree to take part in the research study
- Agree to have the tests and treatments that are described in this ICF
- Agree to the use of your personal and health information as described in this ICF

You may change your mind to no longer take part in this study at any time. You do not need to give a reason and your medical care will not be affected. Your study doctor will want to see you and check your overall health and safety, so please tell your study doctor of your decision before leaving the study.

PURPOSE OF THE STUDY

The purpose of the study is to investigate an experimental drug called voruciclib. Voruciclib is being developed by MEI Pharma Inc. (the Sponsor of this study) as a potential treatment for different types of leukemia, which are forms of cancer that affect immune cells present in the blood, lymph nodes, and other organs. Voruciclib is an investigational drug in the United States because it is not yet approved by the US Food and Drug Administration (FDA).

This study has been designed to look at the safety and efficacy of voruciclib (also known as the study drug), alone, or in combination with venetoclax, how your body tolerates the drug or drug combination, how effective the drug(s) may be, and how the drug is taken up by your body when administered orally after multiple doses over the course of the study.

WHAT IS VORUCICLIB?

Voruciclib blocks a protein called cyclin-dependent Kinase (CDK), which then decreases the amount of another protein called myeloid cell leukemia protein 1 (Mcl-1). Mcl-1 shows up in large amounts in AML cancers. It is thought that blocking Mcl-1 may stop the growth of AML type cancers or enable other drugs to work more effectively.

There is limited information on voruciclib use in humans. To date, voruciclib has been studied in 4 clinical trials (including this one) with approximately 130 patients that had B-cell, AML, or other cancers.

This study is being conducted to determine the lowest safe and effective dose(s) of voruciclib in patients that have relapsed and/or refractory acute myeloid leukemia.

WHAT IS VENETOCLAX?

Venetoclax (Venclexta®) is an approved drug in the U.S. in combination with other drugs for the treatment of newly diagnosed acute myeloid leukemia in adults 75 years or older, or who have other diseases that don't allow for the use of intensive chemotherapy.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 100 subjects are expected to take part in this study at approximately 10 study centers in the United States.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Screening Period

Before you begin the study, you will need to have the following tests or procedures to check on the state of your health and your disease and to assess if you qualify for the study. Most of these tests or procedures will be done within a 28-day period called the Screening Period. Some of them may be part of your regular medical care and may be done even if you do not join the study. In some cases, if you have had some of them recently, they may not need to be repeated.

Screening Period Assessments

The study staff will:

- Discuss this study with you, including your review of this ICF
- Collect information about you, such as your age, sex, race/ethnicity, and your medical history, including assessing symptoms related to your disease
- Review any medications and herbal or dietary supplements you are taking, or have taken, in the last 28 days
- Note: If you have received treatment at another hospital or facility, you may be asked to get a copy of your records for your study doctor
- Perform a physical examination, including blood pressure, heart rate, temperature, height and weight
- Assess your ability to perform everyday tasks
- Conduct an electrocardiogram (ECG): an ECG measures the electrical activity of your heart and requires placement of electrical sensors on your chest, wrists, and ankles. All ECGs are conducted 3 times in a row to make sure the results are consistent.
- Collect approximately 2 to 4 tablespoons of blood and approximately ¼ cup urine to assess your overall state of health, including how your organs are working and to better understand the status of your disease. This will also help to understand how voruciclib in combination with venetoclax works on your cancer type. The following lab tests will also be done:
    - An HIV test: this blood test determines whether you're infected with HIV, a virus that weakens the immune system and can lead to acquired immunodeficiency syndrome (AIDS). Positive test results are required to be reported to local health agencies.
    - Hepatitis B and Hepatitis C test: this blood test is used to detect current or past infection by the hepatitis B or hepatitis C virus, which may cause damage to the liver. Positive test results for hepatitis B and C must be reported to a local health agency.
    - If the HIV or hepatitis tests show infection with these viruses, you will not be able to participate in the study and your study doctor will discuss other treatment options.
    - Cytogenetics (analysis of chromosomes)

- If you are a female of childbearing potential (a woman who can have children), approximately 1 teaspoon of blood will be collected for a pregnancy test. Also, you must use two forms of contraception, one of which should be a barrier contraceptive. Talk to your study doctor to determine if the contraceptives you use meet these requirements.
- Your study doctor may perform tests not required for the study, which may include a blood test or biopsy, to evaluate your disease. If these tests are performed, the results will be collected as part of the study.
- Blood, bone marrow biopsy, or bone marrow aspirate may be collected to evaluate your disease. (Please see **Evaluation of Your Disease** section for more details about this.)

- Chest X-ray may be performed unless recent CT (computerized tomography) scan shows no pulmonary abnormalities.

- **RESEARCH TESTS**

  These tests will be done to better understand how your disease and your immune system may respond to treatment over time and to study which patients may best respond to this treatment in the future. These tests are for measuring Mcl-1 and other proteins involved in preventing the tumor cells from apoptosis (cell death) and may be performed on blood, bone marrow, and other tissue samples.

  All samples collected as part of this research study will be labeled with a study identifier or code that is unique to you and will not be labeled or stored with names or other direct links to your identity. This unique identifier will allow us to link information obtained from your samples and your medical information, but will not enable study personnel to identify you.

  Results from any testing/analysis on your samples will also be labeled with your unique identifier code and will not include your name or other information that could identify you. The confidentiality of any central computer record will be carefully guarded, and no information by which you may be identified will be released or published.

  Your name will not be used in any reports or publications about the research study. No information that may identify you will be released or published.

  The results from these exploratory tests will be used for research purposes only and will not be used in your care. This research will not change the care you receive from your study doctor, but may be useful to guide the treatment of future patients with the study drug.

Voruciclib Dose Level Assignment

After completing the screening procedures, your study doctor will determine your eligibility to take part in this study. If you are eligible, you will be assigned to one of the dosing levels and schedules described below.

Prior to subjects being assigned into the next dose level and schedule cohort, the study doctor and other study personnel will assess the safety of the study drug in the current and prior cohorts.

The study drug dosing level and schedule that you receive will be determined based on when you join the study.

Cohorts 13–19 will receive study drug for the first 2 weeks of each 4-week treatment cycle. By using intermittent scheduling, the hope is to reduce the risk of toxicity (side effects) that was seen when study drug was given on a continuous daily basis.

Cohorts 21–25 will receive study drug for the first 3 weeks of each 4-week treatment cycle. The rationale for this schedule is to decrease the number of days without voruciclib to 7 days in a treatment cycle, thereby reducing the potential risk of AML regrowth during a longer treatment break within a cycle.

The study drug comes in either 50 mg or 100 mg capsules or tablets.

Cohorts 13-19 (Voruciclib and Venetoclax)

The dose of study drug will depend on what cohort you are assigned to, based on the table below. You will be enrolled into one of the groups or cohorts shown below. The enrollment into higher dose cohorts will continue until the safety review committee agrees on a dose that is both safe and effective.

Cohort Dose Level	Doses and Schedule
13	voruciclib 50 mg every day (Day 1–14) + venetoclax (Day 1–28)
14	voruciclib 100 mg every day (Day 1–14) + venetoclax (Day 1–28)
15	voruciclib 150 mg every day (Day 1–14) + venetoclax (Day 1–28)
16	voruciclib 200 mg every day (Day 1–14) + venetoclax (Day 1–28)
17	voruciclib 250 mg every day (Day 1–14) + venetoclax (Day 1–28)
18	voruciclib 300 mg every day (Day 1–14) + venetoclax (Day 1–28)
19	voruciclib 350 mg every day (Day 1–14) + venetoclax (Day 1–28)

Cycle 1 dosing:

- Venetoclax will start with 100 mg on Day 1, and increase to 200 mg on Days 2-21, then 400 mg on Days 22-28.
- Voruciclib dosing will be administered on Days 3-14 at the appropriate Cohort Dose.

Cycle 2 dosing and beyond:

- Venetoclax 200 mg will be administered on Days 1-21, and 400 mg administered on Days 22-28.
- Voruciclib at the Cohort Dose (between 50 mg to 350 mg depending on your assigned cohort) on Days 1-14.

Dosing is summarized in the schedule below. You will be given a dosing diary to help you remember what you are supposed to take each day.

Cohorts 13–19 Administration Schedule of Voruciclib and Venetoclax per 28-day Cycle					
Cycle 1	**Day 1**	**Day 2**	**Days 3 to 14**	**Days 15 to 21**	**Days 22 to 28**
Venetoclax	100 mg	200 mg	200 mg	200 mg	400 mg
Voruciclib (Cohorts 13–19)	None	None	Assigned Cohort Dose (every day)	None	None
Cycle 2 and beyond	**Days 1 to 14**		**Days 15 to 21**		**Days 22 to 28**
Venetoclax	200 mg		200 mg		400 mg
Voruciclib (Cohorts 13–19)	Assigned Cohort Dose (every day)		None		None

Cohorts 21–25 (Voruciclib and Venetoclax)

The dose of study drug will depend on what cohort you are assigned to, based on the table below. The study drug will be taken by mouth. You will be enrolled into one of six groups or cohorts. Once the first cohort to enroll is full, the next cohort will enroll after the study team reviews safety information from the previous cohort. The enrollment into higher dose cohorts will continue until the safety review committee agrees on a dose that is both safe and effective.

Cohort Dose Level	Doses and Schedule
21	voruciclib 150mg every day (Day 1–21) + venetoclax (Day 1–28)
22	voruciclib 200 mg every day (Day 1–21) + venetoclax (Day 1–28)
23	voruciclib 250mg every day (Day 1–21) + venetoclax (Day 1–28)
24	voruciclib 300 mg every day (Day 1–21) + venetoclax (Day 1–28)
25	voruciclib 350 mg every day (Day 1–21) + venetoclax (Day 1–28)

Cycle 1 dosing:

- Venetoclax will start with 100 mg on Day 1, and increase to 200 mg on Days 2–21, then 400 mg on Days 22–28.
- Voruciclib dosing will be administered on Days 3–21 at the appropriate Cohort Dose.

Cycle 2 dosing and beyond:

- Venetoclax 200 mg will be administered on Days 1–21, and 400 mg administered on Days 22–28.
- Voruciclib at the Cohort Dose (between 150 mg to 350 mg depending on your assigned cohort) on Days 1–21.

Dosing is summarized in the schedule below. You will be given a dosing diary to help you remember what you are supposed to take each day.

Cohorts 21–25: Administration Schedule of Voruciclib and Venetoclax per 28-day Cycle				
Cycle 1	**Day 1**	**Day 2**	**Days 3 to 21**	**Days 22 to 28**
Venetoclax	100 mg	200 mg	200 mg	400 mg
Voruciclib QD	-	-	Assigned Cohort Dose (every day)	None
Cycle 2 and beyond	**Days 1 to 21**			**Days 22 to 28**
Venetoclax	200 mg			400 mg
Voruciclib QD	Assigned Cohort Dose (every day)			None

Whichever cohort you are assigned to, there is a possibility that your dose may be decreased, if it is determined that the assigned dose may be unsafe. Additionally, if the safety review committee that oversees this study determines that a higher dose than what you are currently taking appears to be safe and well tolerated, your study doctor may ask you if you would like to increase your voruciclib to a higher dose.

Study Drug Administration

Prior to first dose

Because of the type of drugs voruciclib and venetoclax are, there is a chance that with your first dose you could have symptoms of tumor lysis syndrome (TLS). TLS (rapid death of cancer cells) can occur within 1 to 2 days after starting voruciclib or venetoclax, which if not properly treated can cause severe medical complications, including death. To help reduce your chances of getting TLS, your study doctor will ask that you drink lots of water prior to your first dose. Your study doctor may also prescribe a medication, such as Zyloprim® (allopurinol), to take 2 days prior to your first dose to help reduce any possible risk of getting TLS. In some cases, high risk patients may need to go to the hospital one day prior to your first dose to prevent TLS. Your study doctor will discuss all of this with you and your risk level prior to receiving your first dose of voruciclib. You can find more information regarding the symptoms of TLS further down in this consent under Side Effects of Study Drugs in this Study.

Treatment Phase

For all study participants, the treatment phase starts when study drug is first administered and continues until the last day of study drug administration.

For tracking purposes, study drug administration is broken down into 28-day cycles. For example, Cycle 1 will last from Day 1 through Day 28. Cycle 2 will begin the next day (Cycle 2 Day 1) and last for 28 days. Cycle 3 and all other cycles after will be numbered the same way.

The study drug(s) will be administered by mouth according to the dosing schedule for your cohort.

Voruciclib should be taken on an empty stomach, at least 1 hour prior to food or 2 hours after food at approximately the same time each day. It is recommended that voruciclib be taken in the morning. A missed dose may be taken up to 12 hours after the usual time; after 12 hours the dose should be omitted.

Venetoclax should be taken with a meal and water. When both venetoclax and voruciclib are to be taken, venetoclax should be taken first with a meal followed by voruciclib at least 2 hours later (e.g., meal completed at 8 a.m. with venetoclax, dose of voruciclib taken after 10:00 a.m.). Tablets must not be chewed, crushed, or broken.

On certain days you will be instructed not to take the study drug until after the blood collection at the clinic. Your study doctor will let you know on which days to not take the study drug.

Eating grapefruit or drinking grapefruit juice should be avoided when taking voruciclib, as it may affect the level of drug in the blood.

During the study, your study doctor may change the amount of study drug you are taking, depending on any side effect you may have. You may continue to receive the study drug as long as it continues to be safe and beneficial for you.

You will be given a study diary to record when you take your study drug while at home. The study diary will be given to you each time you are given voruciclib for your next cycle (28 days), and the study staff will teach you how to complete the diary. You will be asked to bring your bottles of voruciclib and venetoclax (even if they are empty), and your study diary to each of your study visits for the site staff to review.

Treatment Period Assessments

If you are eligible to take part in the study, then the following will be done, some of which are part of your regular medical care:

Cycle 1 (Day 1)

- A physical examination, including blood pressure, heart rate, temperature, and weight.
- Your ability to perform everyday tasks will be assessed.
- The study doctor will review how you have been feeling and any medications that you are currently taking.
- ECGs (3 in a row) will be conducted before and after taking study drug(s). Your study doctor will let you know the timing of these ECGs.
- If you are female of childbearing potential, another urine pregnancy test may be performed, depending on when the Screen urine pregnancy test was taken. Your study doctor will let you know if this test will need to be repeated.
- Approximately 2 to 4 tablespoons of blood will be collected to assess your overall state of health, including how your organs are working, to better understand the status of your disease, and to better understand how venetoclax works on your cancer type.
- You will be issued a study drug diary, along with instructions on how to complete it.
- You will be given venetoclax for the remainder of the 28-day cycle.

Cycle 1 (Day 2)

- The study doctor will review how you have been feeling and any medications that you are currently taking.
- Approximately 2 to 4 tablespoons of blood will be collected to assess your overall state of health, including how your organs are working, to better understand the status of your disease.

Cycle 1 (Day 3)

- Approximately 1–2 tablespoons of blood will be taken before and after the first dose of study drug to measure the level of voruciclib and to better understand how voruciclib in combination with venetoclax works on your cancer type.
- You will be given voruciclib for the remainder of the 28-day cycle.

Cycle 1 (Day 4)

- If you are able to make it to the clinic on this day, approximately 1–2 tablespoons of blood will be taken to measure the level of voruciclib.

Cycle 1 (Day 8)

- Depending on how you are feeling you may need a physical examination. Your study doctor will let you know if it is needed.
- Measurements of your blood pressure, pulse, and temperature may be taken.
- The study doctor will review how you have been feeling and any medications that you are currently taking.
- ECGs (3 in a row) will be conducted. Your study doctor will let you know the timing of these ECGs.
- Approximately 2 to 4 tablespoons of blood will be collected to assess your overall state of health, including how your organs are working, to better understand the status of your disease, to measure the level of voruciclib in the blood, and to better understand how voruciclib in combination with venetoclax works on your cancer type.

Cycle 1 (Day 14)

- Depending on how you are feeling you may need a physical examination. Your study doctor will let you know if it is needed.
- Measurements of your blood pressure, pulse, and temperature may be taken.
- The study doctor will review how you have been feeling and any medications that you are currently taking.
- ECGs (3 in a row) will be conducted. Your study doctor will let you know the timing of these ECGs.
- Approximately 4 to 7 tablespoons of blood will be collected to assess your overall state of health, including how your organs are working, to better understand the status of your disease, to measure the level of voruciclib and venetoclax in the blood, and to better understand how voruciclib in combination with venetoclax works on your cancer type.

Cycle 1 (Day 15) Cohorts 13–19 and 21–25

- Approximately 2 to 4 tablespoons of blood may be collected to measure the level of voruciclib and venetoclax in the blood.

Cycle 1 (Day 21)

- Approximately 2 to 4 tablespoons of blood may be collected to measure the level of voruciclib and venetoclax in the blood.

Cycle 2 (Day 1)

- A physical examination, including blood pressure, heart rate, temperature, and weight will be performed.

- Your ability to perform everyday tasks will be assessed.
- The study doctor will review how you have been feeling and any medications that you are currently taking.
- ECGs (3 in a row) will be conducted. Your study doctor will let you know the timing of these ECGs.
- Approximately 4 to 7 tablespoons of blood and approximately ¼ cup urine will be collected to assess your overall state of health, including how your organs are working, to better understand the status of your disease, to measure the level of voruciclib and venetoclax in the blood.
- Urine pregnancy test will be performed if you are a female of childbearing potential.
- You will be issued a study drug diary, along with instructions on how to complete it.
- You will be given voruciclib and venetoclax for the remainder of the 28-day cycle.
- Blood, bone marrow biopsy, or bone marrow aspirate may be collected to evaluate your disease. (Please see **Evaluation of Your Disease** section for more details about this).

Cycle 2 (Day 14)

- The study doctor will review how you have been feeling and any medications that you are currently taking.
- Approximately 2 to 3 tablespoons of blood will be collected to assess your overall state of health, including how your organs are working and to better understand the status of your disease.

Cycles 3 (Day 1) and Beyond

- Depending on how you are feeling you may have a physical examination. Your study doctor will let you know if it is needed.
- Measurements of your blood pressure, pulse, temperature, and weight will be taken.
- Your ability to perform everyday tasks will be assessed.
- The study doctor will review how you have been feeling and any medications that you are currently taking.
- Approximately 2 to 3 tablespoons of blood will be collected to assess your overall state of health, including how your organs are working and to better understand the status of your disease.
- If you are female of childbearing potential, a urine pregnancy test will be performed.
- You will be given a study drug diary, along with instructions on how to complete it.
- You will be given voruciclib for the remainder of the 28-day cycle.
- You will be given venetoclax for the remainder of the 28-day cycle.
- You will follow the same schedule of procedures as listed above for Cycle 3 (Day 1) and for the remainder of your treatment visits. Your visits to the clinic will repeat monthly for as long as you remain on the study.
- Blood, bone marrow biopsy, or bone marrow aspirate may be collected to evaluate your disease. (Please see **Evaluation of Your Disease** section for more details about this).
- On Day 1 and 14 of Cycles 4, 6 and every 3 cycles thereafter, approximately 2 to 4 tablespoons of blood may be collected to measure the level of voruciclib and venetoclax in the blood.

End of Study Visit

You will be asked to return to the clinic for an End of Study Visit approximately 30 days after your last dose of study drug or before starting a new treatment, whichever is earlier.

The following assessments will be completed at this visit:

- A physical examination, including blood pressure, heart rate, temperature, and weight.
- An assessment of your ability to perform everyday tasks.
- A review of how you have been feeling and any medications that you are currently taking.
- ECG (3 times in a row). Your study doctor will let you know the timing of these ECGs.
- Collection of approximately 2 to 3 tablespoons of blood and approximately ¼ cup urine to assess your overall state of health, including how your organs are working, to better understand the status of your disease.

- Urine pregnancy test if you are a female of childbearing potential.
- Tests to evaluate your disease (please see **Evaluation of Your Disease**).
- Blood, bone marrow biopsy, or bone marrow aspirate may be collected to evaluate your disease. (Please see **Evaluation of Your Disease** section for more details about this).

Evaluation of Your Disease

It is considered standard of care to evaluate the status of your disease; which means if you were not taking part in this study, you would still have these types of visits as part of your regular care. Your disease will be evaluated at the study centers at: Screening, at every cycle beginning with Cycle 2 (due to the nature of AML as a rapidly progressing disease), and End of Study.

Depending on your type of cancer and/or your disease status, you may need additional evaluations/tests done. Also, depending on your cancer type, you may have one or more of the below tests done. Your study doctor will let you know which tests you will need done. If it is found that your cancer has become worse, you will be discontinued from study treatment.

All subjects will need blood collected, as described above, and may require a small sample of bone marrow tissue (biopsy) or the liquid portion of the bone marrow (aspirate) that is taken usually from the hip (pelvis) bone. You will first be given a small injection to numb the area. A needle will then be passed through the skin into the bone. A small sample of the bone marrow tissue (biopsy) or liquid (aspirate) will then be drawn into a syringe. It may be painful, but this only lasts for a short time. You may be offered medication before the procedure to reduce any pain or discomfort during the procedure.

- A bone marrow aspirate or biopsy will be taken to assess and classify your disease and/or your potential response to study treatment. These tests will be performed if your study doctor requests them to manage your disease and/or if you have completely responded to treatment. Your study doctor will let you know when to get these tests done.
- You may also need a CT scan of the chest, abdomen, and pelvis. Your study doctor will let you know when to get these scans and/or tests done.

EXPLORATORY RESEARCH

This part of the consent form is about exploratory biomarker research which you can choose to participate in.

It involves allowing analysis of any remaining bone marrow biopsy/aspirate collected for evaluation of your disease.

Bone Marrow Biopsy or a Bone Marrow Aspirate (remaining sample) A portion of the bone marrow biopsy or bone marrow aspirate collected for disease response, may also be sent for further analysis at a central laboratory.

You will not benefit from this research. However, by serving as a participant, other patients with your disease type may benefit in the future. Also, your participation in this part of the study may help your study doctor, including the other Investigators participating in the study, the Sponsor and their affiliates learn more about your disease type.

You can still take part in the study even if you say "No" to this research. If you agree to this research but cannot complete them for any reason, you can still take part in the study.

EXPLORATORY RESEARCH CONSENT:

Please initial below to show whether or not you agree to these procedures.

I give my consent for the use of my remaining **bone marrow /aspirate** for exploratory analysis.

* I understand if I decline the bone marrow aspirate/biopsy exploratory procedure part of the study, I may still need to have a bone marrow aspirate/biopsy performed if my study doctor determines it is needed as part of my patient care and/or to assess whether my tumor is responding to the study drug.

☐ Yes, I agree ☐ No, I decline*

_____

Participant's Initials

HOW LONG WILL I REMAIN ON THIS STUDY?

The length of time that you remain on the study will depend on how well you tolerate study drug and you continue on study drug (up to 5 years). Therefore, your participation in this study will continue until one of the following occurs:

- You withdraw your consent to continue to take part in this research study
- Your cancer becomes worse
- You have severe side effects
- You do not follow the instructions for the study
- The research study ends or is terminated early for any reason
- Other reasons, such as if the study doctor thinks it is in your best interest

Should any of the above occur, your study doctor will discuss this with you along with your options for further treatment.

If you have a serious side effect during the study, the study doctor may ask you to visit the office for follow-up exams even after you have completed your regular study visits.

WHAT ARE MY RESPONSIBILITIES WHILE PARTICIPATING IN THIS STUDY?

- Provide truthful information about your medical history, current conditions, side effects, complaints, and medicines you take, including any supplements or herbal remedies.
- Tell the study doctor about any problems you have during the study
- Take voruciclib (and venetoclax) as directed by your study doctor and complete the study diary
- Show up for all your study visits and bring your study drug bottles (even if empty) and study diary
- Tell your study doctor or office staff if your phone number or address changes
- Tell your study doctor if you are hospitalized at any time during the study and assist with getting your medical records
- Tell your regular doctor or any other doctors or health care providers who treat you while you are in this study that you are in a research study. If you fail to do so, it could put you at significant risk.

CAN I STOP STUDY TREATMENT?

You can decide to stop the study drug at any time without penalty or loss of benefits to which you would be otherwise entitled. Tell the study doctor if you are thinking about stopping. Your study doctor will want to see you to check your overall health and safety before leaving the study.

Your participation in this study may end at any time for medical reasons or because the Sponsor or the US Food and Drug Administration (FDA) finds it necessary to stop this study. The Sponsor and the study doctor are not obligated to provide you with study drug after your participation in the study has ended for any reason.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS OF BEING IN THE STUDY?

You may have side effects from the drug or procedures used in this study and they will vary from person to person. Everyone taking part in the study will be watched carefully for any side effects. However, the study doctor and the study Sponsor may not know all the side effects that may happen. There may be unknown side effects that could occur to you or an embryo or fetus if you (or your partner) become pregnant, which are currently unforeseeable. Side effects can vary from mild to very serious. Your study doctor may give you drugs to help lessen side effects. Many side effects go away soon after you stop taking what is causing them. In some cases, side effects can be serious, long-lasting, and/or may never go away. There is also a rare risk of death. You should talk to your study doctor about any side effects that you have while taking part in the study.

Side Effects of the Drugs Used in this Study

There is limited information on voruciclib use in humans and the long-term side effects of voruciclib is unknown. Voruciclib has been studied in approximately 130 cancer patients at doses ranging from 50 to 850 mg. It is not possible to predict all of the risks and unwanted effects that might happen if you take voruciclib. From the three research studies conducted to date, the longest time a patient was taking the study drug was 11 months. Since the effect of the study drug taken with other medications is unknown, it is important that you tell the study doctor about all prescription and non-prescription drugs, herbal preparations, and nutritional supplements that you are taking or planning to take.

The side effects seen in the research studies conducted to date (which were believed to be possibly related or related to voruciclib) were:

Very Common (≥ 1/10)

- Nausea and vomiting
- Diarrhea
- Fatigue
- Decreased appetite

Common (≥ 1/100 to 1<10)

- Constipation (difficult or hard bowel movements)
- Abdominal Pain and/or Abdominal pain (upper)
- Headache
- Dyspnea (shortness of breath)
- Vertigo and/or Dizziness

- Arthralgia (joint pain)
- Thrombocytopenia (low platelet count; platelets help your blood to clot in an injury)
- Dyspepsia (indigestion)
- Dry mouth
- Hematochezia (blood in stool)
- Stomatitis (inflammation of the mouth and lips)
- Chest pain
- Weight decreased
- Lab Value Changes: [such as Hypokalaemia (low potassium), Hypomagnasaemia (low magnesium), Aspartate aminotransferase (AST) increased (may indicate liver damage), Blood creatinine increased (may indicate kidney damage), International normalized ratio (INR) increased (your blood may take longer to clot with an injury)]
- Dehydration
- Dysgeusia (distortion of the sense of taste)
- Neuropathy peripheral (damage to nerves which feels like numbness or tingling)
- Hematuria (blood in urine)
- Throat irritation
- Skin changes: [such as Dry skin, Pruritus (itchy skin), Rash, Dermatitis Acneiform (acne like bumps on skin)]
- Alopecia (hair loss)
- Hyperhidrosis (excessive sweating)
- Palmar-plantar erythrodysesthesia (hand-foot) syndrome (redness, swelling and pain on palms of hands and/or soles of feet)
- Hypotension (low blood pressure)
- Hypertension (high blood pressure)
- Anxiety

Some but not all uncommon ($\geq$1/1000 to 1<100) side effects which were believed to be related to voruciclib include anemia (low number of red cells), febrile neutropenia (fever with reduction of white blood cells), gastroenteritis (inflammation of the stomach and intestines), infections, prolonged QT interval on electrocardiogram (irregular electrical activity in the heart which could lead to serious abnormal heart rhythms), myalgias (muscle pain), hypoxia (low levels of oxygen in body tissues), inflammation of the lungs (known as pneumonitis or interstitial lung disease), renal (kidney) failure and respiratory failure.

During this study, there have been three cases of inflammation of the lungs (referred to as pneumonitis or interstitial lung disease) believed to be related to voruciclib. The symptoms experienced by these three subjects included difficulty in breathing and shortness of breath that resulted in hospitalization. Symptoms of lung inflammation may also include cough and chest

pain. It is very important that you contact your study doctor if you are having trouble breathing, have a cough or chest pain.

Two of the three cases of lung inflammation were in patients with AML and may have been due to a common reaction to treatment for AML called differentiation syndrome. Symptoms of differentiation syndrome include unexplained fever, weight gain, difficulty breathing, decreased blood pressure, and kidney failure. It is very important that you contact your study doctor if you are experiencing any of these symptoms.

Serious events are those that cause a patient to go into hospital, prolong their stay in hospital, cause disability, be life threatening or fatal. Three patient deaths during participation in a previous voruciclib clinical trial were considered possibly related to the study drug. These patients each received doses of voruciclib higher than those doses being evaluated in this study.

Other drugs that work similar to voruciclib (that is, blocking the CDK protein; ribociclib, palbociclib, abemaciclib) are approved for marketing in the US by the FDA. We do not know if voruciclib will have side effects that are similar to or of the same severity as those seen after treatment with these other drugs. The most severe side effects seen with drugs that block CDK include:

- Severe neutropenia (decrease in certain white blood cells that help fight infections)
- Diarrhea
- Embryo-fetal toxicity (harm to the fetus when administered to a pregnant woman)
- QT interval prolongation (changes to the heart rhythm)
- Hepatobiliary toxicity (increases in liver enzymes)
- Venous thromboembolism (clots in the blood vessels)

Venetoclax

The most common adverse effects that are likely to happen to you from taking Venetoclax are:

- Low white blood cell count (neutropenia)
- Diarrhea
- Nausea
- Low red blood cell count (anemia)
- Upper respiratory tract infection
- Increased risk of infections such as pneumonia and blood infections
- Low platelet count (thrombocytopenia)
- Feeling tired (fatigue)
- Cough
- Muscle and joint pain
- Swelling of your arms, legs, hands, and feet
- TLS (Refer to section below)

Tumor Lysis Syndrome (TLS) (rapid death of cancer cells) may occur within 1 to 2 days after starting voruciclib or venetoclax, which if not properly treated can cause severe medical complications, including death. Symptoms of TLS include nausea, vomiting, weakness, skin swelling, irregular heartbeat, seizures, shortness of breath, muscle cramps, high potassium levels, increase uric acid, kidney failure, and life-threatening heart failure. You may need to be admitted to the hospital for the prevention or treatment of tumor lysis syndrome. During your participation in this study, your study doctor will monitor you closely and prescribe a medication to help your body avoid these types of complications.

Other Potential Risks

Treatment Arm Assignment Risks

You will be assigned to receive treatment with study drug at specific dose levels depending on the dose level (cohort) you are assigned to. The study drug dose you receive may prove to be less effective or to have more side effects than the other dose levels or other available treatment(s) for AML.

Blood Drawing- Risks

During this study, small amounts of blood will be drawn from a vein to perform tests that allow your study doctor to see how you are doing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising and/or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn.

Electrocardiogram (ECG) Risks

The ECG test is a recording of the electrical activity of your heart. The sticky pads used may be cold when applied and sometimes cause some discomfort, such as redness or itching. If the hair under the patches need to be shaved, irritation from shaving could also occur.

Bone Marrow Biopsy or Bone Marrow Aspirate Risks

A small sample of bone marrow tissue (biopsy) or the liquid portion of the bone marrow (aspirate) is taken usually from the hip (pelvis) bone. You will first be given a small injection to numb the area. A needle will then be passed through the skin into the bone. A small sample of the bone marrow tissue (biopsy) or liquid (aspirate) will then be drawn into a syringe. It may be painful, but this only lasts for a short time. You may be offered medication to reduce any pain or discomfort during the procedure.

Though not common, there may be side effects of having a bone marrow aspiration and biopsy such as the following:

- Pressure and/or pain when the needle is inserted, as well as when the bone marrow is removed with a syringe (aspiration)
- Where the needle is inserted into the skin and tissue over the bone, bleeding, bruising, pain, infection may occur

Rare side effects may include the following:

- Infection of the bone
- Extensive bleeding at the biopsy site

Tumor Tissue Biopsy Risks

For a tumor tissue biopsy, the study doctor may make an incision or use a needle to withdraw a sample of your tumor. You may experience the following:

- Excessive bleeding, particularly in people with a low platelet count.
- Infection, especially in people with weakened immune systems.
- Long-lasting discomfort at the tumor biopsy site.

Magnetic Resonance Imaging (MRI) Risks

There are no known biological risks associated with magnetic resonance imaging. Some short-term discomfort may be experienced, including heating, loud noises, and claustrophobia. People with metal objects inside them such as a pacemaker, metal fragments, an aneurysm clip, etc., may not undergo an MRI. Tell your study doctor if you have any metal inside you.

Computerized Tomography/Positron-Emission Tomography (CT/PET Scan) Risks

A radioactive drug (tracer) will be put into your body as a part of a PET scan and an oral (taken by mouth) or intravenous (injected by hypodermic needle into your vein) contrasting agent may be used as a part of a CT scan. Although the amount of radiation that you are exposed to is small and the risk of negative effects from it is low, it may cause an allergic reaction, expose an unborn baby to radiation if you are pregnant, or expose your child to radiation if you are breast-feeding. You may experience slight pain or redness at the injection site, which should resolve.

Reproductive Risks

You should not become pregnant or father a baby while in this study because the drugs in this study on an unborn baby are not known; and could be harmful. Women should not breastfeed a baby while on this study. If you are a woman who can have children (not surgically sterile or post-menopausal), you will have a pregnancy test before you can be in this study. If you are pregnant, you cannot be in this study. Tell the study doctor right away if you suspect that you have become pregnant while in the study. Also, you must either agree to completely abstain from intercourse, or you must use two forms of acceptable birth control, including one barrier method that is approved by your study doctor while you are in the study. Whether you are a man or a woman, you need to use birth control while in this study. Check with your study doctor about the methods of birth control to use and how long to use them.

If you are a man, even if you are surgically sterilized (had a vasectomy) you must use condoms with spermicidal agent for birth control if you choose to have intercourse with women while in this study. You must not donate sperm during the study. If your partner becomes pregnant during this time, the study doctor will ask to collect information about the pregnancy and its outcome. Your partner will be asked to sign a consent form if this occurs.

For more information about side effects and risks, ask your study doctor.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you decide to take part in this study, there is no guarantee that your health will improve. Taking part in this study may or may not make your health better. The information from this study will help the study doctor and the study Sponsor learn more about this study drug as a treatment for AML. This information could help other people who have a similar medical condition in the future.

Because people respond differently, and because the study drug is experimental, you may not benefit from participating in this study. It is possible that your condition may get worse.

WILL I BE TOLD ABOUT NEW INFORMATION?

During the study, you will be told about new information or changes in the study that may affect your health or your willingness to continue on the study. When informed of this new information, if you agree to continue on the study, you will be asked to sign an updated consent form.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Your other choices may include the following:

- Getting other treatment or care for your AML without being in a study. Your study doctor will discuss these available treatment options and how your participation in the study may impact your use of other drugs.
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible

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

WILL I CONTINUE TO RECEIVE THE STUDY DRUG AFTER THE STUDY IS OVER?

The study Sponsor does not intend to continue providing this study drug or any other study treatments to you after the end of the study, or if you choose to withdraw from the study. After your participation in the study ends, you or your health plan will need to pay for medications, clinic, hospital, and doctors' services that are part of your regular medical care.

WILL I BE PAID IF I TAKE PART IN THIS STUDY?

You will not be paid for being in this study and you will not be reimbursed for expenses related to your participation in the study. [Study Site] may pay you a stipend to cover some of your travel costs.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

The study Sponsor, MEI Pharma, Inc., will supply your study drug, voruciclib.

You or a third party will be billed for the costs, study doctor's visits, physical examinations, laboratory testing, medications (specifically venetoclax), bone marrow biopsies, and other procedures used in this study that are considered standard of care. You will receive study drug, voruciclib free of charge. You will be billed for any deductibles or co-payments required by your insurance company or third-party payer. Some insurance companies and third-party payers may not pay for treatment or laboratory tests conducted as part of a research study, including the hospitalization costs. If your insurance company does not pay for these costs, you will be billed for them. You should consult with your health benefit plan to determine whether the costs of care incurred as a result of participating in this study are covered.

Ask your study doctor to discuss the costs that will or will not be covered by the Sponsor. This discussion should include the costs of treating possible side effects. Otherwise, you might have unexpected expenses from being in this study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, [investigator's name(s)], if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him or her at [telephone number].

You will be reimbursed by the Sponsor for any medical expense that you incur as a direct result of the study drug or procedures required under the protocol that are not covered by your insurance company, provided you have followed the instructions of the study doctor.

Money for such things such as lost wages, disability, or discomfort due to research-related injury is not offered.

By signing this informed consent document, you do not give up any legal rights that you otherwise have as a patient in a research study.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

You may choose to either take part or not to take part in the study. No matter what you choose, there will be no penalty to you and you will not lose any of your regular benefits to which you are otherwise entitled. If you do decide to take part in this study, you may leave the study at any time and it will not affect your medical care.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

Your medical information will be kept as confidential as possible within the limits of the law. Your medical information may be given out if required by law. If information from this study is published in a medical journal or presented at scientific meetings, you will not be identified by name, picture, or any other personally identifying information.

The following people and groups of people may look at and/or copy your medical records:

- The Sponsor, their representatives and/or those working for the Sponsor
- The Institutional Review Board responsible for protecting the rights and safety of the patients who take part in research studies
- The U.S. Food and Drug Administration (FDA)

HOW WILL MY HEALTH INFORMATION BE USED AND DISCLOSED?

If you sign this document, you give permission to [Study Site] to use or disclose (share) your health information that identifies you. This information may be shared for the following reasons:

- Purposes of this research study
- Research directly related to AMLand related diseases
- Use of this study drug in disease therapy

This information could be re-disclosed by the recipient and no longer protected.

Your health information includes all that has been and will be created or received by [Study Site] and that is in your medical record kept by [Study Site].

Your authorization (permission) to use and disclose (share) your health information will continue indefinitely, but its use and sharing will only be for the purposes described in this consent form. (or, "Your authorization (permission to use and disclose (share) your health information will expire on _____") {for CA, WA, IN, IL, and WI}

You do not have to sign this consent form. If you choose not to sign it, you may not take part in this research study. You are free at any time to limit [Study Site]'s use and sharing of your health information, without penalty or loss of benefits to which you are otherwise entitled. If at any time you choose to limit [Study Site]'s use and sharing of your health information that is necessary for the completion of this research study, you may not be allowed to take part, or continue to take part, in this research study.

You may change your mind and withdraw your authorization in writing to your study doctor at any time. If you choose to withdraw from the study, no new health information will be collected about you. However, the Sponsor will still be able to use and disclose any health information about you from this research study that has already been collected.

You have the right to see and get a copy of your medical records kept by [Study Site] that are related to the study. However, by signing this consent form you agree that you will not be able to review or receive some of your records related to the study until after the entire study has been completed.

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 Website will include a summary of the results. You can search this Website at any time.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions, complaints, or concerns you have about this study. Contact your study doctor [name(s)] at [telephone number].

For questions about your rights while taking part in this study or if you have any questions, concerns or complaints about the research, contact [Study Site]'s Institutional Review Board or Ethics Committee (a group of people who review the research to protect your rights) at [telephone number].

If at any time during this study you feel that you have not been informed enough about your privacy rights about your health information, or you feel that the privacy of your health information was not protected, you may contact [Study Site's Privacy Office] at [address, telephone number].

SIGNATURE

I have been given a copy of all [insert total number of pages] pages of this form. I have read and understand the information and I have had my questions answered. I agree to take part in this research study and authorize [Study Site] to use and disclose (share) my health information as described in this Informed Consent Form.

_____
Patient Name (print)

_____ _____
Patient Signature Date

I, the undersigned, have fully explained this informed consent to the patient named above.

_____
Name of person conducting informed consent discussion (print)

_____ _____
Signature of person conducting informed consent discussion Date

_____
Witness Name (print) *

_____ _____
Witness Signature * Date

* If the Principal Investigator or Institutional Review Board deems a witness signature is necessary (as per ICH Guidelines, Good Clinical Practice [E6], 4.8.9).

Signature Page for VV-CLIN-000171 v6.0

Approval	Richard Ghalie Medical 30-Jan-2024 22:41:34 GMT+0000

Approval	Ali Hennessey Regulatory 31-Jan-2024 04:24:24 GMT+0000

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