

## SUMMARY OF CHANGES – Consent

**NCI Protocol #:** 10334

**Protocol Version Date:** 11/27/2024

**Protocol Title:** BLockade of PD-1 Added to Standard Therapy to target Measurable Residual Disease in Acute Myeloid Leukemia 1 (BLAST MRD AML-1): A Randomized Phase 2 Study of the Anti-PD-1 Antibody Pembrolizumab in Combination with Conventional Intensive Chemotherapy as Frontline Therapy in Patients with Acute Myeloid Leukemia

**Informed Consent Version Date:** 11/27/2024

### I. Changes by Principal Investigator

#	Section	Comments
1.	All	The date has been changed to match the current version of the protocol.

## Research Study Informed Consent Document

**Study Title for Participants:** Testing the addition of immunotherapy, MK-3475 (pembrolizumab), to conventional therapy for older patients with newly diagnosed acute myeloid leukemia

**Official Study Title for Internet Search on <http://www.ClinicalTrials.gov>:** Protocol 10334, “BLockade of PD-1 Added to Standard Therapy to target Measurable Residual Disease in Acute Myeloid Leukemia 2 (BLAST MRD AML-2): A randomized Phase 2 Study of the Venetoclax, Azacitidine, and Pembrolizumab (VAP) Versus Venetoclax and Azacitidine as First Line Therapy in Older Patients with Acute Myeloid Leukemia (AML) who are Ineligible or who Refuse Intensive Chemotherapy (NCT# TBD)

### Overview and Key Information

#### What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have acute myeloid leukemia (AML) and are ineligible for intensive chemotherapy.

#### Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the “Where can I get more information?” section for resources for more clinical trials and general cancer information.

#### Why is this study being done?

This study is being done to answer the following question:

Will the addition of MK-3475 (pembrolizumab), also known as Keytruda, to azacitidine and venetoclax chemotherapy increase the rate of deeper/better responses and reduce the chance of the leukemia coming back in patients with newly diagnosed AML?

We want to find out if activating the immune system with MK-3475 in addition to the usual chemotherapy is safe and improves the response rate (elimination of leukemia cells) as compared

to what has been reported for usual chemotherapy given in this situation. We are doing this study because we want to find out if this approach is better or worse than the usual approach for your AML. The usual approach is defined as care most people get for newly diagnosed AML.

## **What is the usual approach to my AML?**

The usual FDA-approved approach for patients ineligible for intensive chemotherapy who are not in a study is treatment with a combination of two drugs azacitidine and venetoclax. Among patients aged 60 years and above with adverse genetic risk disease, only 10 out of 100 people are cancer free at 5 years.

## **What are my choices if I decide not to take part in this study?**

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer. This type of care only helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. Comfort care does not treat the cancer directly but instead is meant to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

## **What will happen if I decide to take part in this study?**

If you decide to take part in this study, you will either get azacitidine and venetoclax (usual approach group) for up to 6 cycles, or you will get azacitidine, venetoclax, and MK-3475 (pembrolizumab) (intervention group) for up to 6 cycles. Each treatment cycle will last 28 days. Beyond Cycle 6, if you are responding to study treatment, you will continue to receive azacitidine and venetoclax or azacitidine, venetoclax, and MK-3475 (pembrolizumab) as continuation therapy for: 1) up to 2 years, or 2) until your disease gets worse, or 3) the side effects become too severe, or 4) you decide to stop participating (whichever comes first).

After you finish your treatment, your doctor and study team will watch you for side effects. They will check you in clinic or by phone call every 6 months for up to 3 years after treatment. This means you will keep seeing your doctor for 3 years after treatment.

## **What are the risks and benefits of taking part in this study?**

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

### **Risks**

We want to make sure you know about a few key risks right now. We give you more information in the “What risks can I expect from taking part in this study?” section.

If you choose to take part in this study, there is a risk that the pembrolizumab (MK-3475) may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor’s office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The pembrolizumab (MK-3475) used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you

## Benefits

There is evidence that combining immune system activation and traditional chemotherapy improves outcomes in various cancers. It is not possible to know now if adding the study drug

will improve outcomes compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

## **If I decide to take part in this study, can I stop later?**

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. They will make sure that proper procedures are followed, and a final visit is scheduled to monitor your safety. This will cancel any future research study appointments. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

## **Are there other reasons why I might stop being in the study?**

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

**It is important that you understand the information in the informed consent before making your decision.** Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

## **What is the purpose of this study?**

The purpose of this study is to compare the usual treatment alone to adding MK-3475 (pembrolizumab) to the usual treatment. The addition of MK-3475 (pembrolizumab) to the usual

treatment could improve response rates and induce longer responses to this cancer treatment. But, it could also cause side effects, which are described in the risks section later.

This immune system activating drug, MK-3475 (pembrolizumab), is already approved by the FDA for use in several cancers. However, MK-3475 (pembrolizumab) is not approved by the FDA or known to be safe for use in AML either alone or in combination with standard chemotherapy. The drug is given every 3 weeks and is typically used after the standard front-line drugs have stopped working.

This study will help the study doctors find out if this different approach is better than the usual approach. To decide if it is better, the study doctors will be looking to see if the addition of pembrolizumab results in fewer detectable leukemia using new methods.

There will be about 76 people taking part in this study.

## **What are the study groups?**

This study has 2 study groups. You will be told which group you are in.

- Group 1**

If you are in this group, you will get the usual study drugs, azacitidine at 75 mg/m<sup>2</sup>/day through a vein in your arm or beneath your skin on Days 1-7 and venetoclax at 400 mg/day orally on Days 1-28 of the first cycle and on Days 1-21 or Days 1-28 of each cycle thereafter depending on the results of your blood count. If you are unable to receive azacytidine over the weekend, your doctor may give it to you for 5 days in week 1 and 2 days in week 2. If you derive a clinical benefit within the first 6 cycles of therapy, you will continue with the second part of therapy that consists of the same combination for up to 2 years provided you do not stop responding at any time during the second part of therapy.

There will be about 38 people in this group.

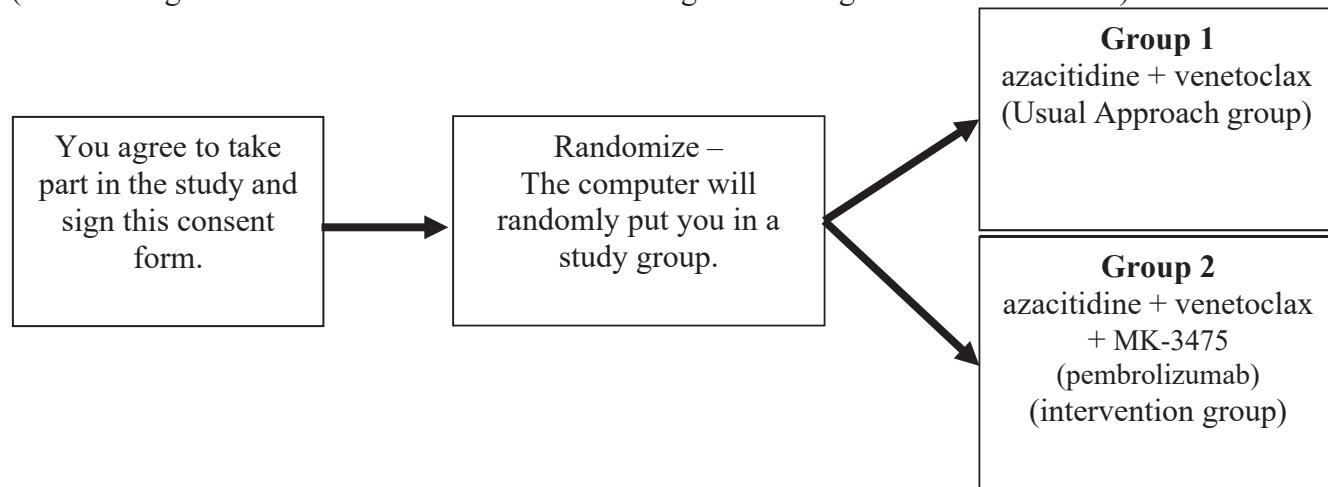
- Group 2**

If you are in this group, you will get the usual study drugs, azacitidine at 75 mg/m<sup>2</sup>/day through a vein in your arm or beneath your skin on Days 1-7 and venetoclax at 400 mg/day orally on Days 1-28 of the first cycle and on Days 1-21 or Days 1-28 of each cycle thereafter depending on the results of your blood count. If you are unable to receive azacytidine over the weekend, your doctor may give it to you for 5 days in week 1 and 2 days in week 2. You will receive MK-3475 (pembrolizumab) through a vein in your arm on Day 8 of the first cycle and every 3 weeks thereafter. This drug is not approved by the FDA for treatment of your disease. If you derive a clinical benefit within the first 6 cycles of therapy, you will continue with the second part of therapy that consists of the same combination for up to 2 years provided you do not stop responding.

There will be about 38 people in this group.

We will use a computer to assign you to one of the study groups. This process is called “randomization.” It means that your doctor will not choose, and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2

Another way to find out what will happen to you during this study is to read the chart below (start reading at the left side and read across to the right following the lines and arrows).



### What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Blood tests before the study starts, on Days 1 through 4 of the first cycle, Day 28 of the first cycle, day 1 of all cycles, and at the end of treatment.
- In Group 2, blood tests, and thyroid testing will be performed before you begin treatment and <3 days prior to each dose of MK-3475 (pembrolizumab). Additional thyroid testing (T3 and T4) will be performed as your doctor says it is necessary to do so.

- Bone marrow biopsy and aspirate after Cycles 1, 4, and 6 of 1<sup>st</sup> part of therapy (induction phase) and after 1 year of treatment, and if your disease gets worse.
- Bone marrow biopsy and aspirate after Cycle 2 if your disease has not improved after Cycle 1.
- During the second part of therapy that consists of the same combination of medications for up to 2 years, provided you do not stop responding, there will be an optional bone marrow biopsy and aspirate every 3 months.

If you agree, collection of left-over samples from your bone marrow samples will be discussed in the section on optional studies. The increased volume collections will have no patient impact.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

You will need to have additional bone marrow aspirations and biopsies for the study. This sample is a required part of the study. The study takes a small amount of bone marrow from your body. This is like the bone marrow aspiration and biopsy you had that helped diagnose your cancer. These collections will be done before you start treatment, and the bone marrow after completion of Cycle 2. If bone marrow cannot be obtained, your study doctor will let you know if you are still able to participate in the study.

Stool samples will be taken for the study. A stool sample will be collected before starting treatment. An additional stool sample will be taken at the end of the first cycle of therapy.

Blood samples will also be taken for the study. The blood samples will be collected on the same days as the bone marrow aspirations.

Bone marrow aspirate and blood samples will be tested to determine your response to therapy. Additional optional studies include new methods for detecting leftover leukemia cells and predicting your response to therapy. You and your study doctor will not get the results of this testing.

Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA that may occur during treatment. You and your study doctor will not get any results of this testing. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

A skin punch biopsy before you begin treatment.

A patient study calendar is attached at the end of this document. It shows how often these tests and procedures will be done.

## **What risks can I expect from taking part in this study?**

### **General Risks**

If you choose to take part in this study, there is a risk that adding MK-3475 (pembrolizumab) to the standard drugs azacitidine and venetoclax may not be better than the usual “azacitidine and venetoclax” approach for your cancer at improving the response rates.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- May not be able to take part in future studies.

The study drugs used in this study may have adverse effects on a fetus in utero. Furthermore, it is not known if MK-3475 (pembrolizumab) has transient adverse effects on sperm. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 120 days after you have completed the study. If you inadvertently become pregnant while on treatment with MK-3475 (pembrolizumab) or within 120 days of the last dose of study treatment, you need to call the study doctor immediately. Do not breast-feed while you take this drug or for 120 days after your last dose.

### **Genetic Testing Risks**

The genetic test used in this study will test your tumor for genetic alterations in frequently mutated genes in AML. Rarely, these genetic changes also may be present in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what testing your normal tissue may mean for you and your family. He or she also may suggest that you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for any genetic tests and visits to a genetic counselor done outside of this study.

### **Biopsy Risks**

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. The biopsy needle will go through the skin into the bone and may produce a brief, sharp pain. Since the inside of the bone cannot be numbed, this procedure may cause some discomfort, however not all patients experience discomfort. The possible side effects associated with a bone marrow biopsy include pain, bleeding, bruising, and infection, as well as a reaction to the numbing agent. Pain can be treated with regular pain medications.

Common risks of a skin punch biopsy are a small amount of bleeding at the time of the procedure, bruising, pain, the possibility of an adverse reaction consisting of local swelling, bleeding, infection, and scar formation at the biopsy site. There also could be a small risk of infection. The pain associated with injection of a local anesthetic is mild and transitory. Allergic reactions to lidocaine, a local anesthetic cream, are extremely rare (less than 1 in 10,000).

Occasionally, patients may get swelling at the injection site. Significant bleeding from the biopsy site(s) is rare and infrequent. A small scar will result at the biopsy site.

### **Blood Draw Risks**

You may feel discomfort during some of the tests or procedures during this study or may experience some inconveniences. Some of the risks from drawing blood from your arm may include pain, bruising, lightheadedness, and rarely, infection. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

### **Side Effect Risks**

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

### **Allergy Risk**

All drugs have a potential risk of allergic reaction. Allergic reactions may range from mild (rash, hives) to severe (difficulties to breath, blood pressure collapse). A severe allergic reaction needs immediate attention and could result in permanent disability or death.

## Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

**Study Group 1 and Group 2** – Possible side effects of azacitidine and venetoclax are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

### Possible Side Effects of Azacitidine

(Table version date: July 30, 2019)

<b>COMMON, SOME MAY BE SERIOUS</b>	
In 100 people receiving azacitidine, more than 20 and up to 100 may have:	
• Anemia which may require blood transfusion	• Constipation, diarrhea, nausea, vomiting
• Tiredness, fever	• Swelling and redness at the site of the medication injection
• Infection, especially when white blood cell count is low	• Bruising, bleeding
<b>OCCASIONAL, SOME MAY BE SERIOUS</b>	
In 100 people receiving azacitidine, from 4 to 20 may have:	
• Heart failure which may cause shortness of breath, swelling of ankles, and tiredness	• Fluid around heart
• Abnormal heartbeat	• Pain
• Difficulty swallowing or sleeping	• Bleeding from multiple sites including nose
• Internal bleeding which may cause black tarry stool, blood in vomit or coughing up blood	• Sores in the mouth
• Chills	• Weight loss, loss of appetite
• Swelling of arms, legs	• Muscle weakness
• Dizziness, headache	• Worry, confusion
• Hair loss, itching, rash	• Cough, shortness of breath, postnasal drip
• Low blood pressure which may cause feeling faint	
<b>RARE, AND SERIOUS</b>	
In 100 people receiving azacitidine, 3 or fewer may have:	

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Kidney damage which may cause swelling, may require dialysis

### Possible Side Effects of Venetoclax

(Table Version Date: May 8, 2019)

#### COMMON, SOME MAY BE SERIOUS

In 100 people receiving venetoclax (ABT-199), more than 20 and up to 100 may have:

- Anemia which may require blood transfusion
- Diarrhea, nausea
- Tiredness
- Infection, especially when white blood cell count is low

#### OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving venetoclax (ABT-199), from 4 to 20 may have:

- Constipation, vomiting
- Fever
- Bruising, bleeding
- Pain in joints
- Headache
- Cough
- High blood pressure which may cause headaches, dizziness, blurred vision

#### RARE, AND SERIOUS

In 100 people receiving venetoclax (ABT-199), 3 or fewer may have:

- Kidney damage which may require dialysis

**Study Group 2** - In addition to side effects listed above, people who are in Group 2 may also have some side effects from MK-3475 (pembrolizumab). These side effects are listed below.

### Possible Side Effects of MK-3475 (pembrolizumab)

(Table Version Date: August 14, 2024)

#### COMMON, SOME MAY BE SERIOUS

In 100 people receiving pembrolizumab (MK-3475), more than 20 and up to 100 may have:

- Tiredness

#### OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving pembrolizumab (MK-3475), from 4 to 20 may have:

- Nausea
- Loss of appetite
- Pain in back
- Joint stiffness
- Swelling and redness of the skin

Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Anemia which may require blood transfusion
- Pain in lymph nodes
- Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Diarrhea
- Sores in the mouth which may cause difficulty swallowing
- Pain in belly
- Sores in the bowels
- Chills, fever
- Reaction during or following a drug infusion which may cause fever, chills, rash, low blood pressure
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Pain or swelling of the joints
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives

**RARE, AND SERIOUS**

In 100 people receiving pembrolizumab (MK-3475), 3 or fewer may have:

- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss
- Inability to digest food which may cause bloating
- Swelling of the gall bladder
- Swelling of the spinal cord
- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: Shortness of breath, swelling of the ankles and body.
- Swelling and redness of the eye which may cause blurred vision with a chance of blindness
- Swelling of the bowels
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin
- Damage to organs in the body when the body produces too many white cells
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in a coma
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs.
- Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures and stiff neck
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure
- Swelling or tenderness of blood vessels

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

## Additional Drug Risks

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

## What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  1. all medications and supplements you are taking
  2. any side effects
  3. any doctors' visits or hospital stays outside of this study
  4. if you have been or are currently in another research study.

**For women:** Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 120 days after your last dose of study drug.

## What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the azacitidine and venetoclax ready and giving it to you. You or your insurance provider will have to pay for azacitidine and venetoclax while you take part in this study.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study which are not standard of care. These include:

- The bone marrow biopsies and aspirations before you start treatment; induction (during the first part of therapy) at Cycle 2 if your disease has not improved after Cycle 1.
- Blood sample collections as a part of research studies at the beginning of the study, 1

year after treatment, when your disease returns, and at the end of the study or when your disease gets worse.

- The skin punch biopsy before you begin study treatment

There will be no charge to you or your insurance provider for the MK-3475 (pembrolizumab). There will be no charge to you or your insurance provider for tests or procedures noted with an asterisk (in the study calendar) as these are performed for study purposes only. All other tests and procedures will be charged to you or your insurance provider in the usual way as these are standard of care. This may include other tests and procedures not listed in this consent if your doctor feels it is necessary for your care, such as additional laboratory tests for monitoring your safety.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

\*\*\*You will be responsible for paying for the procedure if any or all the standard of care bone marrow samples are not reimbursed by your insurance company.

## **What happens if I am injured because I took part in this study?**

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

## **Who will see my medical information?**

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal

information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The U.S. Department of Health and Human Services (DHHS) agencies
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

## Where can I get more information?

You may visit the NCI web site at <http://cancer.gov/> for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (\*insert name of study doctor[s]\*) at (\*insert telephone number, and email address if appropriate\*).

For questions about your rights while in this study, call the (\*insert name of organization or center\*) Institutional Review Board at (\*insert telephone number\*).

### **Optional studies that you can choose to take part in**

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with AML in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say “no” to any or all of these studies. There is no penalty for saying “no.” You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of “yes” or “no” for each of the following studies.

### **Optional sample collections for unknown laboratory studies and/or storage for possible future studies**

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person’s response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

## Unknown future studies

If you choose to take part in this optional study, blood and bone marrow will be collected and stored. Storing samples for future studies is called “biobanking.” The biobank is being run by Nationwide Children’s Hospital in Columbus, Ohio, and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people’s health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don’t know what research may be done in the future using your blood and bone marrow samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

## What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. Bone marrow biopsies and about 2 additional tablespoons of bone marrow will be collected from your bones on the first day of the study, during the first part of therapy (induction phase) after the 4<sup>th</sup> cycle, after the 6<sup>th</sup> cycle, after 1 year of treatment, every three months during the second part of therapy (continuation therapy to try to keep the remission), or if you stop responding to treatment and will be sent to the biobank.
2. About 2 teaspoons of blood will be collected every three months during the second part of therapy (continuation therapy to try to keep the remission).
3. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.

4. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
5. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

### **What are the risks in this optional sample collection?**

- The most common risks related to a bone marrow aspirate is a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection, significant bleeding, or collapsing of the lung can occur.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance.
- Generally, hospitals will keep some of your tissue and blood. This tissue may be used to help treat your cancer in the future. There is a small risk that when these samples are submitted to the biobank for this optional sample collection, your samples could be used up.

### **How will information about me be kept private?**

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. Only your study doctor and a few study researchers will have access to the master list linking the code numbers to names. The biobank and the genomic sequencing laboratory will receive your samples with the following information only: your sample code number; your age, race/ethnicity, and gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

### **What are the benefits to taking part in this optional sample collection?**

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

### **Are there any costs or payments to this optional sample collection?**

There are no costs to you or your insurance for exams, tests, and procedures done for research purposes only; these include the bone marrow biopsy, blood draw, and biobanking of your specimen(s). You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

### **What if I change my mind about this optional sample collection?**

If you decide you no longer want your samples to be used, you can call the study doctor, (\*insert name of study doctor for main trial\*), at (\*insert telephone number of study doctor for main trial\*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

### **What if I need my tissue or blood samples to be returned?**

Tumor tissue or blood samples that remain in the biobank can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be returned if tissue is needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Tumor tissue or blood samples and genetic material (DNA and RNA) that is no longer in the biobank or that has already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

### **What if I have questions about this optional sample collection?**

If you have questions about the use of your samples for research, contact the study doctor, (\*insert name of study doctor for main trial\*), at (\*insert telephone number of study doctor for main trial\*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

#### **Samples for unknown future studies:**

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES

NO

**This is the end of the section about optional studies.**

**My signature agreeing to take part in the study**

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

**Participant's signature**

Date of signature

**Signature of person(s) conducting the informed consent discussion**

Date of signature

## Study Calendar

		First Part of Therapy (Induction Phase)																					
		Cycle 1						Cycle 2-6															
Before the Study														End of Study/ When your disease gets worse		Post-Treatment Follow-Up <sup>a</sup>							
Pre-Study	Before Treatment	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 14	D 28	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 1	D 2	D 28	Days 1-28
EKG (Assessment after Pre-Study taken as your doctor indicates it is necessary)																							
Assessment of the size, shape, and position of the heart																							
Vital signs and physical exam																							
Blood or urine collection																							
Pregnancy Test																							
Medications you are currently taking																							X







