Research Study Informed Consent Document

Study Title for Participants: Testing pembrolizumab with existing cancer therapy in patients with evidence of residual Chronic Myelogenous Leukemia.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: EA9171, "A Phase II Study of adding the anti-PD-1 antibody pembrolizumab to tyrosine kinase inhibitors in patients with chronic myeloid leukemia and persistently detectable minimal residual disease" (NCT03516279)

Version Date: March 2, 2020

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. 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 chronic myelogenous leukemia (CML).

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:

What are the good and bad effects of adding the study drug pembrolizumab to the usual treatment for patients with chronic myelogenous leukemia (CML)?

We are doing this research study because we want to find out if this approach is better or worse than the usual approach for this type of cancer. The usual approach is defined as care most people get for CML and includes treatment with tyrosine kinase inhibitors (TKIs). The combination of pembrolizumab with the TKIs you are already taking could shrink your cancer, but it could also cause side effects. Researchers hope to learn if the research study drug will shrink the cancer/prevent it from returning. Pembrolizumab has already been approved by the U.S. Food & Drug Administration (FDA) to treat other cancers. There will be about 40 people taking part in this research study.

What is the usual approach to my chronic myelogenous leukemia (CML)?

CML is a rare form of leukemia that used to be lethal in most patients unless they underwent allogeneic hematopoietic stem cell transplantation. The introduction of a group of drugs called tyrosine kinase inhibitors (TKI) has improved the outcomes of patients dramatically and many patients now live many years. You have already been treated with a class of drugs called tyrosine kinase inhibitors (TKI). You are currently being treated with one of those TKIs: imatinib (gleevec), dasatinib (sprycel) or nilotinib (tasigna). These are all approved by the FDA. However, there is still evidence of leukemia cells in your body by laboratory measurement. The response to therapy in CML is measured by the level of a fusion gene product called bcr-abl in your blood. Although you might be feeling well and your blood counts might be completely normal, bcr-abl remains detectable in your blood, which is called minimal residual disease (MRD). As therapy with TKIs does not lead to cure, the current standard of care is for patients to remain on TKI treatment lifelong as long as they are responding and not having significant side effects. When patients lose response to one particular TKI or develop significant toxicity, they can be switched to another TKI. Despite having MRD, the survival on TKI therapy is very good.

If bcr-abl is undetectable in the blood, a patient is considered to have undetectable minimal residual disease (UMRD). UMRD means we cannot detect evidence of leukemia in the body. However, we know from research that almost all patients still have leukemia cells in them even when the bcr-abl does not detect leukemia

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.

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

If you decide to take part in this study, you will get study drugs for up to 2 years.

After you finish your study treatment, your doctor will continue to follow your condition at least every 6 months and watch you for side effects. You will continue to see your doctor for up to 6 years after you start this study.

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 addition of pembrolizumab may not be as good as the usual approach at shrinking your cancer.

There is also a risk that you could have side effects from the pembrolizumab. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Pembrolizumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. Some of the most common side effects that the study doctors know about are:

- Intestinal problems that can rarely lead to tears or holes in your intestine. Signs and symptoms could include: diarrhea or increase in bowel movements, severe belly pain or tenderness, or blood in your stools
- Hormone gland problems. Signs and symptoms could include: headaches that will not go away, extreme tiredness, changes in mood or behavior, decreased sex drive, or weight loss or gain
- Reaction to drug infusion that could lead to a fever, chills, or rash
- Liver problems which can rarely cause liver failure. Signs and symptoms could include: yellowing or your skin or whites of your eyes, severe nausea or vomiting, drowsiness, or pain in the right upper belly
- Lung problems. Signs and symptoms could include: new or worsening cough, chest pain, or shortness of breath

- Skin problems including itching, acne, rash, hives, or blisters and peeling on the skin or mouth.

There may be some risks that the study doctors do not yet know about.

Benefits

This study drug pembrolizumab has shrunk your type of cancer in a limited number of people with your cancer. It is unlikely that it will work in everyone with your cancer or help you live longer. However, it may help the study doctors understand how this study drug works and learn things that may help other 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. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change or risk to your health. 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 National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (ECOG-ACRIN). 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 research study is to test any good and bad effects of the study drug called pembrolizumab. The combination of pembrolizumab with the TKIs you are already taking could shrink your cancer but it could also cause side effects. Researchers hope to learn if the

research study drug will shrink the cancer /prevent it from returning. Pembrolizumab has already been FDA-approved to treat other cancers. There will be about 40 people taking part in this research study.

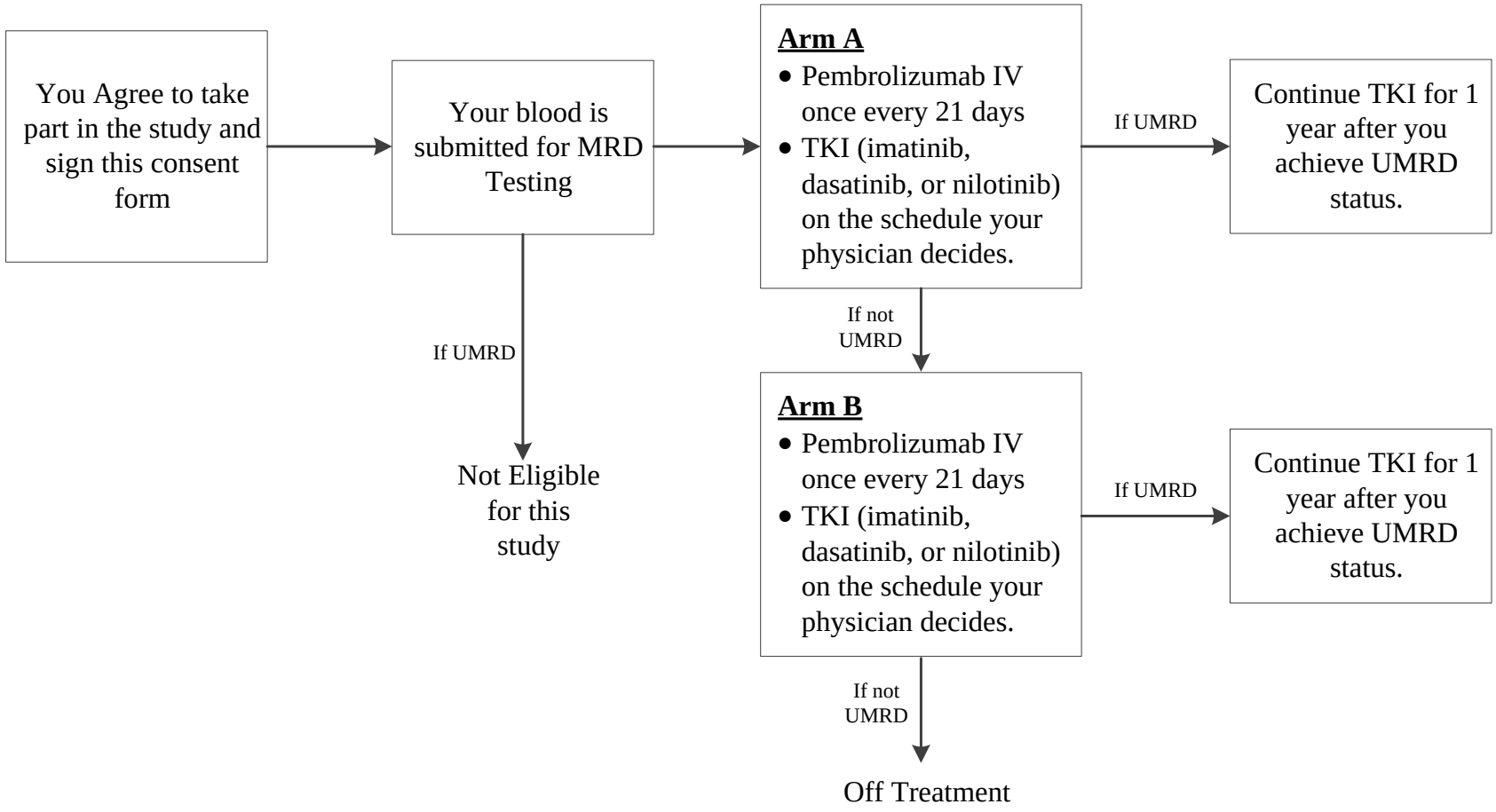
What are the study groups?

All study participants will be on Arm A and receive pembrolizumab intravenously every 3 weeks for 18 doses. This means that you will receive an infusion through your vein over approximately 30 minutes once every 3 weeks for a total duration of about 1 year (54 weeks). During that time, you will continue to take the TKI you were on prior to joining the study.

After completing 54 weeks of treatment combining the TKI, which you were taking prior to entering this study, plus pembrolizumab, a decision regarding your further treatment strategy will be made depending on whether bcr-abl remains detectable in your blood or not.

- If bcr-abl becomes undetectable at end of the first year of combined therapy, you will stop receiving pembrolizumab and will continue just on the TKI. If bcr-abl remains undetectable in your blood for a year, then you would stop taking your TKI and we will monitor serial bcr-abl levels from your peripheral blood for 2 years to assess whether bcr-abl remains undetectable. On the other hand, if bcr-abl becomes detectable in your blood again, you will start back on a TKI and will be taken off treatment.
- If bcr-abl remains detectable in your blood after the first year of combined therapy in the study, you will continue to Arm B and receive both TKI and pembrolizumab for another year. After an additional year of pembrolizumab, we will check your bcr-abl levels in the blood again. If there is no evidence of bcr-abl in the blood, you will stop taking your TKI and we will observe you for an additional 2 years. On the other hand, if you still have detectable bcr-abl in your blood, you will be taken off the combination treatment.

Another way to find out what will happen to you during this research 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.

Before you begin the study:

You will need the following extra tests and procedures to find out if you can be in the research study:

- Pregnancy test (if you are a woman of childbearing potential)
- Blood tests
- Blood will be sent to a central laboratory for Minimal Residual Disease (MRD) assessment.
- Bone marrow biopsy to confirm your cancer diagnosis.

The results of the MRD assessment will be sent to your doctor and will be placed in your medical record, which may affect your care.

The results of the MRD assessment will be used to determine if you can take part in this study.

- If the MRD test results are negative (undetectable), you will be taken off study.
- If the MRD test results are positive (detectable), you will be registered to the study.
- Patients who are negative MRD at or prior to cycle 17 testing must continue treatment through cycle 18 before discontinuing pembrolizumab.

During the study:

- Blood tests during every cycle, when/if you achieve UMRD, and immediately after study treatment. One cycle is equal to 21 days.
- Blood will be sent to a central laboratory for Minimal Residual Disease (MRD) assessments.
- The results of the MRD assessments will be sent to your doctor and will be placed in your medical record, which may affect your care.

- A bone marrow must be performed at Step 0 Screening, time of TKI discontinuation, time of progression and study discontinuation. It is optional to be performed every 3 months during treatment and should follow institutional standard of care.

The blood will be collected by using a needle to draw some blood from your vein. Blood will be collected (approximately two [2] teaspoons) every twelve (12) weeks [every four (4) cycles, prior to pembrolizumab dose] during combined pembrolizumab and TKI therapy, every four (4) weeks for the first six (6) months post TKI discontinuation, then every eight (8) weeks for the subsequent six (6) months post TKI discontinuation, and then every twelve (12) weeks for one (1) year.

If you agree, any leftover blood will be stored for Bio-banking (see Section on Optional Studies).

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:

- The pembrolizumab and TKI combination may not be as good as the usual approach at shrinking your cancer.
- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss.
- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with 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.
- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.
- There can be mild pain, or some bleeding and bruising when blood is drawn. Rarely, an infection can happen where the needle was placed. Feeling dizzy or faint can also happen, but should only last a few minutes after the blood is drawn.
- You may not be able to take part in future studies.

The study agent pembrolizumab used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. 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.

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. Pain can be treated with regular pain medications. Rarely, an infection can occur. A numbing agent that can cause a stinging or burning sensation will be injected at the site of your bone marrow biopsy. The biopsy needle will go through the skin into the bone and may produce a brief, sharp pain. As the bone marrow liquid is taken from the bone, there may be a brief, sharp pain.

You may sign a separate consent form for the study biopsy that describes the risks in more detail.

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.

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.

Possible Side Effects of MK-3475 (pembrolizumab) (CAEPR Version 2.5, December 27, 2019):

Pembrolizumab (MK-3475) can cause your immune system to attack normal organs and tissues in many areas of your body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death. Getting medical treatment right away may help keep these problems from becoming more serious. Your doctor will check you for these problems during treatment with Pembrolizumab (MK-3475). Your doctor may treat you with corticosteroids or other therapy or may need to delay or completely stop treatment if you have severe side effects.

Call or see your doctor right away if you develop any symptoms of the following problems or these symptoms get worse:

Lung problems (pneumonitis). Symptoms of pneumonitis may include:

- shortness of breath
- chest pain
- new or worse cough

Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include:

- diarrhea or more bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems (hepatitis). Signs and symptoms of hepatitis may include:

- yellowing of your skin or the whites of your eyes
- nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- dark urine
- feeling less hungry than usual
- bleeding or bruising more easily than normal

Hormone gland problems (especially the thyroid, pituitary, adrenal glands, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:

- rapid heart beat
- weight loss or weight gain
- increased sweating
- feeling more hungry or thirsty
- urinating more often than usual
- hair loss

- feeling cold
- constipation
- your voice gets deeper
- muscle aches
- dizziness or fainting
- headaches that will not go away or unusual headache

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:

- change in the amount or color of your urine.

Problems in other organs. Signs of these problems may include:

- rash
- changes in eyesight
- severe or persistent muscle or joint pains
- severe muscle weakness
- low red blood cells (anemia)

Infusion (IV) reactions, that can sometimes be severe and life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- shortness of breath or wheezing
- itching or rash
- flushing
- dizziness
- fever
- feeling like passing out

COMMON, SOME MAY BE SERIOUS In 100 people receiving MK-3475 (pembrolizumab), more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving MK-3475 (pembrolizumab), from 4 to 20 may have:
• Nausea • Infection • Loss of appetite • Pain in back

OCCASIONAL, SOME MAY BE SERIOUS

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

- Joint stiffness
- Cough
- Swelling and redness of the skin

MK-3475 (pembrolizumab) 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
- 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
- Fluid in the joints
- Pain in chest
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives

RARE, AND SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), 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
- Swelling of the spinal cord
- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

MK-3475 (pembrolizumab) 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
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Reaction during or following a drug infusion which may cause fever, chills, rash
- 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
- 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

The study drug could interact with other drugs and food, including grapefruit products and Seville oranges. Your study doctor will talk to you about these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

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

In addition, like any study involving stopping the TKI for patients with CML, there is a risk that your disease will come back. In other discontinuation studies, around 60% of patients with CML who stopped TKI had reappearance of bcr-abl and needed to go back on TKI therapy. Most patients for whom bcr-abl reappeared, this occurred within the first 6 months of stopping TKI therapy, but it can happen later as well. While it is theoretically possible that the CML will come back in aggressive fashion, previous studies have shown that with close monitoring and restarting the TKI therapy, almost all patients were able to achieve good control of the CML. However, we still do not yet understand their long-term outcomes.

Finally, while we do not typically observe significant lowering of blood counts with pembrolizumab and we have no reason to suspect that combining pembrolizumab with TKI will cause or worsen cytopenias (low blood counts), this combination has not yet been tested and cytopenias could happen. If that happens, low platelet count can lead to bleeding, low neutrophil count can lead to infections, and low hemoglobin (anemia) can cause fatigue and tiredness. Your blood counts will be monitored closely during the study, and we expect that we would be able to manage the low blood counts if they occur by temporarily or permanently stopping the study drugs and/or supportive care (transfusions, antibiotics, etc.).

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.

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:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - 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.
- 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. These include:

- scheduled MRD assessments

You or your insurance provider will not have to pay for the pembrolizumab while you take part in this study.

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.

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. Contact information for your study doctor is listed on the consent cover page. 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.

No funds have been set aside to compensate you in the event of injury.

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.

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study.

There are organizations that may look at 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:

- Montana Cancer Consortium
- The study sponsor and drug company supplying the study agent (pembrolizumab) now or in the future.
- The 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 NCI's National Clinical Trials Network and the groups it works with to conduct research.

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 information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, call the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

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 this optional study hope the results will help other people with cancer 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 this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

Optional sample collections for biobanking 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, samples of your bone marrow will be collected and stored and leftover samples of your blood will be stored. Storing samples for future studies is called "bio-banking." The biobank is being run by ECOG-ACRIN 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.

We don't know what research may be done in the future using bone marrow and your blood 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.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.

- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

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

1. Approximately one (1) teaspoon of bone marrow aspirate will be collected prior to the start of treatment to be stored in the biobank. The bone marrow collection is to occur at the time of your diagnostic biopsy.
2. Your leftover blood samples from the MRD assessments (described above) and some related health information 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.
3. Researchers can only get samples from the biobank after their research has been approved by experts. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use samples for research. All research projects using these samples will also be reviewed by an ethics or institutional review board to ensure that the request is necessary and proper. Researchers will not be given your name or contact information.
4. 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?

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. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

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 samples 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.
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.

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. 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, who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. Then, any samples that remain 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 have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

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:

May we have samples of your bone marrow for future research?

- **I agree to provide additional samples for research.**

YES NO

May we keep any blood leftover from the mandatory laboratory research studies for future research?

My samples and related 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 the optional study where I circled "yes".

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)

(Required for initial consent only)