SUMMARY OF CHANGES

NCI Protocol #: 10367
Local Protocol #: PhI-115
Protocol Version Date: December 21, 2021

Protocol Title: A Phase 1b Study with Expansion Cohort of Escalating Doses of KRT-232 (AMG 232) Administered in Combination with Standard Induction Chemotherapy (Cytarabine and Idarubicin) in Newly Diagnosed Acute Myelogenous Leukemia (AML)

Informed Consent Version Date: December 21, 2021

Summary of Changes (4/21/21 version to 12/21/21 version)

#	Section	Change
1.	Face page	Changed version date to December 21, 2021.
2.	[redacted]	[redacted]
3.	What exams, tests, and procedures are involved in this study? Study Calendar	Updated the 2 sections to match the protocol for the additional sample that may be taken.
4.	ICD What are the study groups?	Food-effect on KRT-232 exposure is no longer applicable. KRT 232 can be taken with a full glass of water with or without food. Please reconcile. **PI Response:** Done

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of an anti-cancer drug, KRT-232 (AMG 232), to the usual treatments (Cytarabine and Idarubicin) in patients with Acute Myeloid Leukemia

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10367, A phase 1b study with expansion cohort of escalating doses of KRT-232 (AMG 232) administered in combination with standard induction chemotherapy (cytarabine and idarubicin) in newly diagnosed acute myelogenous leukemia (AML) (NCT# NCT04190550)

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 newly diagnosed acute myeloid leukemia (AML).

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:

Is the study drug (KRT-232 [AMG 232]) when given along with the usual combination of drugs (cytarabine and idarubicin) safe and tolerable in patients with acute myeloid leukemia, and what is the safest and most tolerable dose of KRT-232 (AMG 232) when used in this combination?

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 AML.

This is the first time these drugs will be tested together in humans.

What is the usual approach to my Acute Myeloid Leukemia (AML)?

The usual approach for patients who are not in a study is treatment with chemotherapy. Both usual treatments, cytarabine and idarubicin, have been approved by the Food and Drug Administration (FDA) for your type of cancer.

The study drug, KRT-232 (AMG 232), is not approved by the FDA for treating any type of cancer when used alone or in combination with the usual AML treatments (cytarabine and idarubicin).

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 the study drug, KRT-232 (AMG 232) by mouth daily for 7 days of a 28-day cycle in combination with the usual chemotherapy drugs, cytarabine and idarubicin, for up to 2 cycles.. You will receive the study drug until your disease progresses, or the side effects become too severe. Since the study medication has the potential to interact with other medications, you will be given a drug information handout and wallet card as a resource for yourself and your other caregivers.

About 4 weeks after you finish your treatment, your doctor will check on any side effects during a doctor visit. If you stop the study but your disease has not gotten worse, you will have a bone marrow aspirate/biopsy assessment of your AML every 3 months for 2 years until your disease gets worse or you begin a different treatment. After that, the doctor or study team will follow up every six months (either in person or by phone call).

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 study drugs may not be as good as the usual approach alone at stabilizing your cancer.

There is also a risk that you could have side effects from the study drug. These side effects may be worse and may be different than you would get with the usual approach for your cancer. Combining the study drugs can result in greater similar side effects of those currently experienced by each drug individually.

Some of the most common side effects that the study doctors know about are:

- Diarrhea, nausea, vomiting
- Bruising, bleeding
- Loss of appetite

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

Benefits

There is some evidence in animals that adding KRT-232 (AMG 232) to the usual approach can stabilize cancer for longer than the usual approach alone. However, we do not know if this will happen in people. It is unlikely that this KRT-232 (AMG 232) will help you live longer than the usual approach alone. This study may help the study doctors 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. 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 test the safety and tolerability (side effects) of adding a study drug called KRT-232 (AMG 232) at different doses to standard treatment with cytarabine and idarubicin. "Dose" is defined as the amount of drug you get, such as 120mg. We want to find out what effects the drug has on people, if any. Another purpose of the study is to check the level of the study drugs in your blood (pharmacokinetics). In addition, another objective of the study is genetic testing using your tumor tissue to see if the combination of drugs may work in treating your type of cancer. There will be about 34 people taking part in this study.

What are the study groups?

There are two parts in this study, a dose escalation part and a dose expansion part. Your doctor will tell you which part you are in. You will receive the study drugs in the hospital while you are there for the usual AML treatment.

In the dose escalation part of this study, different people will get different doses of the study drug KRT-232 (AMG 232) along with cytarabine and idarubicin.

The first three people taking part in this study will get the starting dose. If the drug does not cause serious side effects, the next group of people in the study will get a higher dose. The study doctor will watch each group carefully as they increase the dose. The doses will continue to increase for every new group until people have serious side effects that require the dose to be lower. Once this dose is found, the dose escalation is stopped.

In the dose expansion part of this study, the highest dose with manageable side effects will be given to up to 12 more people along with cytarabine and idarubicin. This will help study doctors better understand the side effects that may happen with this drug.

Treatment schedule: You will only receive the study drug, KRT-232 (AMG 232), along with cytarabine and idarubicin during the first cycle and second cycle of treatment (if a second cycle is given to you). If you are given additional doses of cytarabine and idarubicin alone in the

middle of the first cycle, then you will not be eligible to receive a second cycle of the study drug along with cytarabine and idarubicin.

You will get KRT-232 (AMG 232) as a pill you take by mouth for the first 7 days of each cycle. You can take KRT-232 (AMG 232) with a full glass of water with or without food. Do not crush or chew the tablets. You will also get cytarabine as a continuous infusion through a vein in your arm for the first 7 days and idarubicin for 3 days. The cycle lasts 28 days. If you have benefitted from the treatment but you still have signs of AML, you can receive additional doses of only cytarabine and idarubicin in the middle of cycle 1 to treat the residual AML. Alternatively, if you have benefitted from the treatment, but you did not receive the additional doses of only cytarabine and idarubicin in the middle of cycle 1 and you still have signs of AML at the end of cycle 1, you may receive a second cycle of cytarabine, idarubicin, and KRT-232 to treat the residual AML. If you have no signs of AML in response to treatment, the second part of therapy may be given to you with Cytarabine on Days 1, 3, and 5 (total of 6 doses) and repeated every 28 to 35 days for 3 to 4 additional cycles. See the study calendar for more information.

You will not be able to get additional doses of KRT-232 (AMG 232). This drug is not approved by the FDA for treatment of your disease.

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:

- EKG done before the study
- Blood counts done weekly during each cycle.
- Physical exams done on the first and fourth week of each cycle.

This study will use genetic tests that may identify changes in the genes in your DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If the changes in your genes were inherited, the changes could also affect the health of your family members.

You and your family may want to know about any genetic test findings that may be important to your health. You may use this form to grant us permission in advance to give this information to your doctor. If a genetic test result about you seems to be medically important and you have granted us permission to contact you, the following steps will occur:

1. Researchers will study the result further to decide if it may be medically important to you or your relatives.
2. The research laboratory that performed the genetic test will contact your doctor about the finding. The research laboratory, which will not have any identifying information about you, will provide your doctor with a code number assigned to your genetic test sample.
3. Your doctor will use the code number to identify you, and will then contact you about the medically important finding. Your doctor may try to contact you several times.
4. You will require another genetic test to confirm the results. This test must be paid for at your own expense.
5. If it is confirmed that there are changes found that could cause health problems, then your doctor will discuss your options with you. We strongly suggest that you also talk to a genetic counselor. Genetic counseling services must be paid for at your own expense.

It is more likely, however, that you will not be contacted by us about a medically important finding. Even if we do not contact you, it does not mean that your genes do not contain changes that are important to your health. Researchers are always learning about new and medically important changes in genes and some information may be learned in the future. Researchers will only decide to contact you about genetic test results at the time your DNA is initially sequenced. You will not be contacted or consented for any research done using your samples in the future, and you will not receive any reports or information about any medically important findings learned in the future. Also, sometimes the meaning of genetic test results can be uncertain, and we may not know for sure what the results mean for your future health. Sharing an uncertain genetic test result with you could offer little benefit, no benefit at all, or could even be harmful.

Results from genetic testing will not be a part of your medical records, unless the results are confirmed by additional testing that you agreed to. See "Who will see my medical information?" for laws and risks in protecting your genetic information.

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 biopsies of your bone marrow for the study. The study biopsy takes a small amount of bone marrow fluid from your body through a needle inserted into the bone. This is like the biopsy you had that helped diagnose your cancer and we will collect your first biopsy sample from the time of your diagnosis of AML. The first biopsy will be done before you begin the study drug. Biopsies will also be done on day 14 and on day 28 after you take the KRT-232 (AMG 232). Another bone marrow biopsy may be done on day 28 of the 2nd cycle to

confirm no signs of AML in response to treatment so that the second part of therapy may be given to you. Bone marrow biopsies may also be done at follow up visits. The bone marrow collections are mandatory for the study. If the study doctors are unable to get a sample of your bone marrow, they may be able to use blood instead.

Blood samples will also be taken and are mandatory for the study to see how the body absorbs, distributes, and gets rid of the study drugs and for other genetic purposes. The first two blood samples will be collected before you receive the study drug. Additionally, a total of six additional blood samples will be collected on the first day at 1, 3, 5, 6, 8, and 24 hours after you receive the study drug KRT-232 (AMG 232).

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 the KRT-232 (AMG 232) may not be as good as the usual approach for your cancer at stabilizing your cancer.

You also may have the following discomforts:

- Lose time at work or home and 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 study drug 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 5 weeks (for women) and 3 months (for men) after you have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Genetic Testing Risks

As part of this study, we are also studying a genetic test. The test is designed to find out if your tumor does not have a change in the gene for TP53. If it does not have a change, you will be assigned to a study group.

Because this genetic test is still being studied, there is a risk that the test results may be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option for you. Or, you may not be included in this study even though it may offer a good treatment option for you.

Bone Marrow Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, swelling, scarring at the wound site, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection or significant bleeding can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Side Effect Risks

The study drug 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 drug.

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:

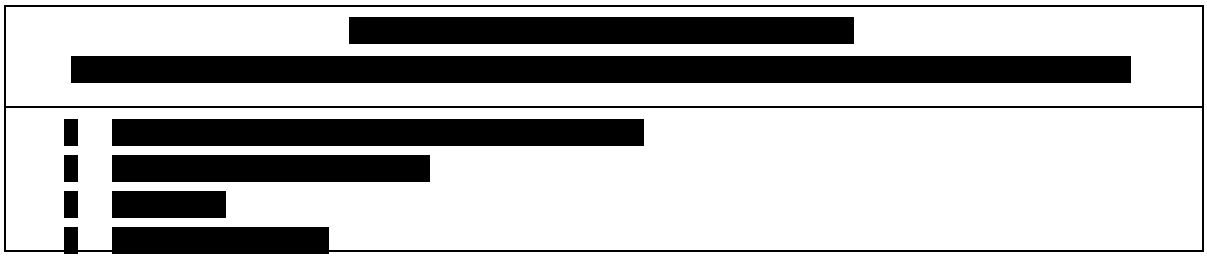
- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

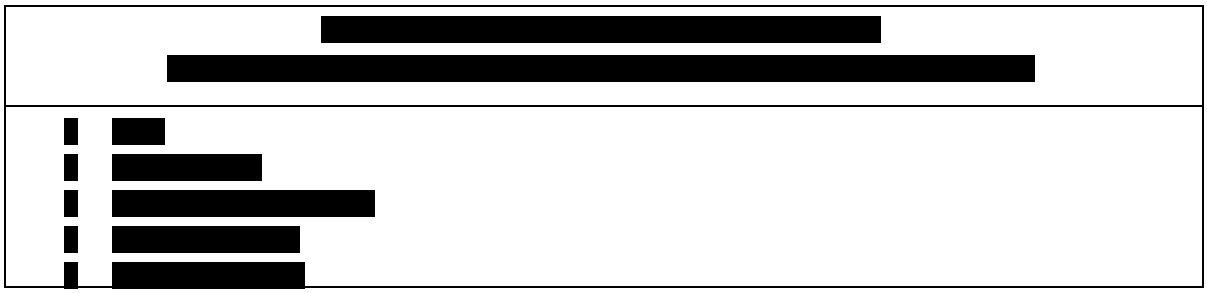
This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects compared to using the study drug or chemotherapy alone. In particular, bruising and bleeding (associated with a decrease in the blood cells that help your blood to form clots) and infections, especially when the white blood cell count is low, may be increased by the drug combination. These side effects may be life-threatening.

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.

[redacted]





Possible Side Effects of Cytarabine
(Table Version Date: July 27, 2015)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cytarabine, more than 20 and up to 100 may have:
• Blood clot • Rash • Swelling in the rectum which may cause rectal pain • Diarrhea, loss of appetite, nausea, vomiting • Sores in mouth which may cause difficulty swallowing • Anemia which may cause tiredness, or may require blood transfusions • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cytarabine, from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Numbness and tingling of the arms and legs • Severe blood infection • Kidney damage which may cause swelling, may require dialysis • Headache • Dizziness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cytarabine, from 4 to 20 may have:
• Chest pain • Hair loss • Liver damage which may cause yellowing of skin or eyes • Swelling and redness of the eye

RARE, AND SERIOUS In 100 people receiving Cytarabine, 3 or fewer may have:
• Coma

Possible Side Effects of Idarubicin
(Table Version Date: October 10, 2017)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Idarubicin, more than 20 and up to 100 may have:
• Pain • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require transfusion • Headache • Diarrhea, nausea, vomiting • Hives • Redness, pain or peeling of palms and soles • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Idarubicin, from 4 to 20 may have:
• Heart failure or attack which may cause shortness of breath, swelling of ankles, and tiredness • Abnormal heartbeat • Liver damage which may cause yellowing of eyes and skin • Sores in mouth which may cause difficulty swallowing • Reddish discoloration of the urine, sweat and saliva • Swelling and redness at the site of injection • Swelling and redness at the site of previous radiation • Loss of nails • Darkening of the skin and nails

RARE, AND SERIOUS In 100 people receiving Idarubicin, 3 or fewer may have:
• Cancer of the bone marrow (leukemia) caused by chemotherapy • Kidney damage which may require dialysis

Additional Drug Risks

The study drug could interact with other drugs. Your study doctor will give you a drug information handout and wallet card that lists 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.

[redacted]

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 within3 months after your last dose of study treatment.

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 cost of treatment with cytarabine and idarubicin
- the costs of getting the KRT-232 (AMG 232), cytarabine and idarubicin ready and giving it to you.
- your insurance co-pays and deductibles.
- the bone marrow collections standard of care at pre-study, day 14, and day 28 or when your bone marrow counts return to normal.

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:

- Research blood draws before you receive the study drug and on the first day of the cycle at 1, 3, 5, 6, 8, and 24 hours after you receive the study drug.

You or your insurance provider will not have to pay for the KRT-232 (AMG 232) 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. 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, the coordinating center California Cancer Consortium Data Coordinating Center, and any drug company supporting the study or the study agent 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.

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 sample collections for known 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 or bone marrow will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the University of Southern California 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/or tissue 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.

If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

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

1. The blood and bone marrow that was previously collected will be sent to the biobank.
2. 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.
3. Researchers can only get samples from the biobank after their research has been approved by experts. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request to use the materials stored in the

Biobank. There will also be an ethics review 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?

- The most common risks related to a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain and scarring at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection or significant bleeding can occur. The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- 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 can also be a risk in knowing genetic information. New health information about inherited traits might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

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. 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 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

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

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

			Cycle 1						Cycle 2*						
	Pre-study	Before you receive the study drug	D1	D3	D7	D14	D21	D28	D1	D3	D7	D14	D21	D28	Off-Study Evaluation
KRT-232 (AMG 232)[a]			X----------X						X----------X						
Cytarabine[b]			X----------X						X----------X						
Idarubicin[c]			X----------X						X----------X						
Pre-study procedures, including, informed consent, demographics, medical history, and height	X														
Physical exam and vital signs	X				X			X			X			X	X
Weight	X				X		X				X		X		X
Assessment of how well you perform every-day tasks and activities	X				X						X				X
Blood draws for complete blood count and general health status	X				X	X	X	X			X	X	X	X	X
EKG (as your doctor indicates is necessary)	X														
Pregnancy test	X														

			Cycle 1						Cycle 2*						
	Pre-study	Before you receive the study drug	D1	D3	D7	D14	D21	D28	D1	D3	D7	D14	D21	D28	Off-Study Evaluation
Bone marrow collection for standard of care assessment	X					X[d]		X[d]						X[d]	
Bone marrow collection for research purposes		X	X[e]			X[e]		X[e]						X[e]	X[e]
Blood collection for research purposes			X												

* If you have benefitted from the treatment but you still have signs of AML, you can receive additional doses of only cytarabine and idarubicin in the middle of cycle 1. Alternatively, if you have benefitted from the treatment, but you did not receive the additional doses of only cytarabine and idarubicin in the middle of cycle 1 but you still have signs of AML at the end of cycle 1 you may receive a second cycle of cytarabine, idarubicin and KRT-232. If you have no signs of AML in response to treatment, the second part of therapy may be given to you with Cytarabine on Days 1,3, and 5 (total of 6 doses) and repeated every 28 to 35 days for 3 to 4 additional cycles.

a: KRT-232 (AMG 232): dose as assigned, given on days 1-7.

b: Cytarabine: dose as assigned, given daily by IV on days 1-7.

c: Idarubicin: dose as assigned, given daily by IV on days 1-3.

d: Your study doctor will decide if you have a bone marrow collection on Day 14 of Cycle 1, Day 28 of Cycle 1, Day 28 of Cycle 2 or when your bone marrow counts return to normal.

e: A blood draw may be performed instead.