Protocol #: 10076
Local Protocol #: NCI10076
Protocol Version Date: 01/15/2024

Protocol Title: A Phase 1 Dose-Escalation and Exploratory Dose Expansion Study of KRT-232 (AMG 232) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone in Relapsed and/or Refractory Myeloma

THIS AMENDMENT IS BEING SUBMITTED IN RESPONSE TO REQUEST FOR RAPID AMENDMENT (RRA) FROM DR. LORRAINE PELOSOF (CTEP MEMO DATED ON 12/29/2023)

#	Section	Page(s)	Change
1	**Header**	all	Version date updated from 01/24/2022 to 01/15/2024

2	**Risks**	5-6	*Per revised KRT-232 CAEPR – Version 2.4, December 8, 2023, modified risk language as per below:*
			• *Increase in Risk Attribution:*
			  • Changed to Common from Occasional: Loss of appetite
			  • Changed to Occasional from Also Reported on KRT-232 Trials But With Insufficient Evidence for Attribution (i.e. added to Risk Profile): Infection, especially when white blood cell count is low; Weight loss; Dizziness; Headache
			• *Decrease in Risk Attribution:*
			  • Changed to Occasional from Common: Bruising, bleeding
			  • Changed to Also Reported on KRT-232 Trials But With Insufficient Evidence for Attribution from Occasional (i.e. removed from risk list): Swelling of arms, legs
			• Provided Further Clarification:
			  • Pain (under Occasional) is now captured as Belly pain (under Occasional).

THE FOLLOWING ARE PREVIOUS CTEP AMMENDMENT RECOMMENDATIONS FROM PREVIOUS CTEP AMENDMENT APPROVAL MEMO DATED 03/23/2021

#	Section	Page(s)	Change
1	**Study Groups**	2	In the third paragraph, please edit KRT-232 (AMG-232) administration as shown below.

#	Section	Page(s)	Change
			KRT-232 (AMG 232) is taken ~~by mouth on an empty stomach at least 2 hours after a meal and 2 hours~~ ~~before the next meal~~ with a glass ~~(240 mL)~~ of water with or without food. **PI Response:** Completed

Consent Form

Study Title for Study Participants: Testing the addition of KRT-232 (AMG 232) to usual chemotherapy for relapsed multiple myeloma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10076. A Phase 1 Dose-Escalation and Exploratory Dose Expansion Study of KRT-232 (AMG 232) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone in Relapsed and/or Refractory Myeloma

What is the usual approach to my relapsed Multiple Myeloma?

You are being asked to take part in this study because your Multiple Myeloma has come back. The usual therapy did not keep your cancer from coming back. Doctors typically give people with your type of cancer several types of chemotherapy that is FDA approved.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above with a chemotherapy regimen that is FDA-approved such as carfilzomib, lenalidomide, and dexamethasone (KRd) alone.
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

The purpose of this study is to test the safety of a study drug called KRT-232 (AMG 232) when used in combination with a standard treatment regimen that is used to treat relapsed or refractory multiple myeloma called carfilzomib, lenalidomide, and dexamethasone (KRd). KRT-232 (AMG 232) has been tested in humans in studies for other cancers.

To accomplish this goal, different doses of KRT-232 (AMG 232) will be tested to see which dose is safer in people when used with standard doses of carfilzomib, lenalidomide, and dexamethasone.

Another purpose of this study is for researchers to learn whether a biomarker can help predict which patients will respond well (have tumor shrinkage) from the combination of KRT-232 (AMG 232) and KRd.

There will be about 25-40 people taking part in this study.

What are the study groups?

If you are found to be eligible to take part in this study, you will be assigned to a study group based on when you join this study. A range of 15 to 30 participants will take part in Part 1 of this study to determine the best dose. Three 3 to 6 participants will be enrolled per group. Approximately 10 participants with relapsed and/or refractory multiple myeloma will be enrolled in Part 2 of the study.

If you are enrolled in Part I, different doses of the study drug KRT-232 (AMG 232) will be given to several study participants in combination with standard doses of carfilzomib, lenalidomide, and dexamethasone.

KRT-232 (AMG 232) is with a full glass of water with or without food. Carfilzomib is given through your vein. Lenalidomide is taken by mouth with or without food. Dexamethasone is either given through your vein or is taken by mouth. A pill diary will be provided to ensure that are taking your medications by mouth as instructed.

The first several study participants will receive the lowest dose of KRT-232 (AMG 232). If the KRT-232 (AMG 232) does not cause serious side effects, it will be given to other study participants at a higher dose. The doses will continue to increase for every group of study participants until side effects occur that require the dose to be lowered.

If you are enrolled in Part 2, you will receive KRT-232 (AMG 232) at the dose that was tolerated in combination with carfilzomib, lenalidomide, and dexamethasone in Part 1.

How long will I be in this study?

You will receive KRT-232 (AMG 232) in combination with carfilzomib, lenalidomide, and dexamethasone for up to 18 cycles which is approximately 18 months (1 cycle = 4 weeks), followed by KRT-232 (AMG 232), lenalidomide, and dexamethasone as long as you are tolerating the treatment and your myeloma is being controlled by the combination of drugs which is tested by the usual treatment criteria. After you finish your treatment, your doctor will continue to watch you for side effects and follow your condition for 30 days.

You may also be removed from the study depending on the results of genetic testing on your myeloma that will be performed at the time of study enrollment. The results of this testing may give us information on whether or not KRT-232 (AMG 232) has a chance to be effective in your myeloma, although the results of this testing may not be available until after you begin therapy. If the results of this testing show that it is unlikely you would benefit from KRT-232 (AMG 232), you will be removed from the study after the first cycle (4 weeks) of treatment with KRd + KRT-232 (AMG 232), and you will continue on KRd alone as per the standard treatment for relapsed or refractory myeloma. In the event you are removed from the study, you will still be followed for potential side effects of KRT-232 (AMG 232) for a minimum of 30 days after you are removed from the study.

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 extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests and procedures that you will need to have if you take part in this study.

Before you begin the study:

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

- Echocardiogram
- Myeloma bone survey which are X-rays of the bones
- Buccal (inner cheek) mucosal swab
- Bilateral (from both sides of hip) bone marrow biopsy and aspiration to remove small pieces of cancer tissue. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study. The material from the biopsy will be used to evaluate the status of the disease and to assess biomarkers that may predict response to therapy. To collect a bone marrow biopsy and aspirate, an area of the hip or other site is numbed with anesthetic and a

small amount of bone marrow and bone is withdrawn through a large needle. Cytogenetic testing looks at how genetic changes to cells may affect how the disease may react to the study drug. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.

During the study:

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the additional procedures and tests performed for research purposes. They are not part of the usual approach for your type of cancer. A study calendar that shows how often these exams, tests, and procedures will be done is attached.

- Blood samples (about 6 tablespoons total) will be collected to measure the concentration of KRT-232 (AMG 232) in your blood before your first dose of KRT-232 (AMG 232) and 5 more times over the next 24 hours. This will only occur on Cycle 1, Day 1 of the study.
- Blood samples (about 2 tablespoons total) will be collected for biomarker testing two times: once before your first dose of KRT-232 (AMG 232) and once 24 hours later. This will only occur on Cycle 1, Day 1 of the study.

At the end of the study:

- Unilateral (from one side of hip) bone marrow biopsy and aspiration to remove small pieces of cancer tissue. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study. The material from the biopsy will be used to evaluate the status of the disease and to assess biomarkers that may predict response to therapy. To collect a bone marrow biopsy and aspirate, an area of the hip or other site is numbed with anesthetic and a small amount of bone marrow and bone is withdrawn through a large needle. Cytogenetic testing looks at how genetic changes to cells may affect how the disease may react to the study drug. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.

If you agree, leftover genetic material from your bone marrow biopsy may be stored for biobanking for future research studies. This will be explained in the optional studies section of this consent document.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Results of the testing will be available to you and your study doctor.

Neither you nor your health care plan/insurance carrier will be billed for the extra research testing and procedures that will be done for this study.

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

If you choose to take part in this study, there is a risk that the KRT-232 (AMG 232) + Carfilzomib, Lenalidomide, and Dexamethasone (KRd) 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 KRT-232 (AMG 232) 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."

Please insert this condensed risk profile as the Table of Possible Side Effects for KRT-232 (AMG 232) in your ICD.

COMMON, SOME MAY BE SERIOUS In 100 people receiving KRT-232 (AMG 232), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Tiredness • Loss of appetite

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving KRT-232 (AMG 232), from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Belly pain • Constipation • Bruising, bleeding, weight loss • Dizziness, headache • Change in taste

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.

A drug information leaflet and wallet card for the potential drug-interactions will be provided to you.

Possible Side Effects of Lenalidomide

COMMON, SOME MAY BE SERIOUS In 100 people receiving lenalidomide (CC-5013), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Constipation, diarrhea • Tiredness • Bruising, bleeding

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving lenalidomide (CC-5013), from 4 to 20 may have:

- Infection, especially when white blood cell count is low
- Dizziness, fainting
- Blurred vision
- Cloudiness of the eye, visual disturbances
- Pain
- Dry mouth, skin
- Heartburn, nausea, vomiting
- Chills, fever
- Swelling of the body
- Fall
- Weight loss, loss of appetite
- Dehydration
- Muscle weakness
- Abnormal unpleasant sensation, body movement
- Changes in taste
- Headache
- Feeling of "pins and needles" in arms and legs
- Numbness, tingling or pain of the arms and legs
- Depression
- Difficulty sleeping
- Change in mood
- Cough, shortness of breath
- Nose bleed
- Increased sweating
- Itching, rash
- Sores on the skin
- High blood pressure which may cause headaches, dizziness, blurred vision
- Low blood pressure which may cause feeling faint
- Blood clot which may cause swelling, pain, shortness of breath

RARE, AND SERIOUS

In 100 people receiving lenalidomide (CC-5013), 3 or fewer may have:

- Abnormal heartbeat
- Heart attack, heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Liver damage which may cause yellowing of eyes and skin, swelling
- 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
- Kidney damage which may require dialysis
- Damage to muscle which may cause muscle pain, dark red urine
- Cancer of bone marrow caused by chemotherapy
- Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions
- Increased tumor size
- A new cancer unrelated to an earlier cancer
- A new cancer resulting from treatment of earlier cancer
- Stroke which may cause paralysis, weakness
- Damage to the lungs which may cause 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
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body
- Difficulty stimulating enough stem cells in the bloodstream for future transplant

Possible Side Effects of Carfilzomib, Lenalidomide, and Dexamethasone (KRd)

Possible side effects of Carfilzomib, Lenalidomide, and Dexamethasone, which is a standard approach for this type of cancer include the following:

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carfilzomib, Lenalidomide, and Dexamethasone, more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Decreased white blood cell count, which can increase the risk of infection • Bruising, bleeding • Diarrhea • Tiredness • Cough • Fever • Upper respiratory infection • Electrolyte abnormalities in the blood • Muscle spasms

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carfilzomib, Lenalidomide, and Dexamethasone, from 4 to 20 may have:
• Constipation • Nausea or vomiting • Swelling of the arms or legs • Bronchitis • Pneumonia • Shortness of breath • Numbness and tingling • Rash • Difficulty sleeping • Elevated blood sugar levels • Elevated blood pressure • Kidney failure • Heart failure • Heart disease such as coronary artery disease • Blood clots • Heart disease

RARE, AND SERIOUS In 100 people receiving Carfilzomib, Lenalidomide, and Dexamethasone, 3 or fewer may have:
• Second primary cancer • Severe lung toxicity, which can result in death • Liver failure, which can result in death • Posterior Reversible Encelophalopathy Syndrome (PRES), which is a neurologic disorder which can cause seizures, headaches, confusion, visual disturbances, and high blood pressure • Severe infusion reactions, which can be life-threatening

Infusion reactions, including life-threatening reactions, have been reported in patients receiving carfilzomib. Symptoms of an infusion reaction may include fever, chills, body aches, facial flushing, vomiting, weakness, shortness of breath, low blood pressure, passing out, chest tightness. These reactions can occur immediately following or up to 24 hours after administration of carfilzomib.

You will need to take oral valacyclovir (or an equivalent antiviral medication) for the duration of treatment to help prevent viral infections while on carfilzomib therapy,

You will need to take pantoprazole (or equivalent medication) to help prevent stomach ulcers while on dexamethasone therapy.

You will need to take aspirin (or other similar medication at your doctor's disrection if you are intolerant to aspirin) for the duration of treatment to help prevent blood clots while on lenalidomide and dexamethasone.

Sedation Medication Side Effects

You may receive your bone marrow biopsy and aspiration under sedation if you prefer. Sedative medicines may make you sleep for several hours and sometimes can have prolonged effect. You will need to have someone take you home after receiving sedation for your bone marrow biopsy. Uncommon but serious complications include: irregular heartbeat, increases or decreases in blood pressure, rare reactions to medications used, and blockage of breathing passages. All of these complications are treatable but rarely, may lead to coma or even death. Emergency personnel and equipment will be available in the event of a serious adverse reaction to sedation. You will have an opportunity to discuss these risks and the specific drugs that will be used with the nurse or doctor who will supervise the sedation.

Other Risks

Bone marrow biopsies/aspirations performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies/aspiration. This may be performed under sedation if you prefer. An allergic reaction to the anesthetic may occur. A scar may form at the biopsies/aspiration site. You will sign a separate consent form before the biopsy is taken. This will be a standard bone marrow biopsy and aspiration consent form from the institution where the biopsy procedure takes place.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions .

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

Genetic testing on myeloma cells obtained from your bone marrow aspirations performed while your are on the clinical study will be performed as part of the planned research studies to idenfity potential biomarkers that may predict response to therapy. There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique 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 or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that 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.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The drugs used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

Because taking part in this study can result in risks to an unborn or breastfeeding baby, you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

In particular, due to the pregnancy related risks of lenalidomide, you will will need to enroll in a lenalidomide Risk Evaluation and Mitigation Strategy (REMS) program, which is a drug safety program that is required by U.S. Food and Drug Administration (FDA) with lenaldidomide use. As part of the REMS program, you will need to take a telephone survey prior to each dispensment of a lenalidomide prescription. If you are a premenoapusal female, a pregnancy test will be required and confirmed to be negative prior to each dispensment of a lenalidomide prescription.

Birth Control Specifications:

Males: Men treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 3 months after completion of KRT-232 (AMG 232) administration. If your partner becomes pregnant or suspects pregnancy, you should inform your treating physician immediately.

Females: Women of child-bearing potential must agree to use adequate contraception prior to study entry and for the duration of study participation through 5 weeks (women) after receiving the last dose of KRT-232 (AMG 232). Should you become pregnant or suspect you are pregnant while you or your partner is participating in this study, you should inform your treating physician immediately.

Women using oral contraceptives or a hormonal method of contraception associated with a risk of thrombosis should consider an alternative method of effective contraception during treatment with study drugs. Your doctor will discuss alternative approaches with you.

Adequate methods of effective birth control include sexual abstinence (men, women); vasectomy; or a condom with spermicide (men) in combination with barrier methods, hormonal birth control or IUD (women).

What possible benefits can I expect from taking part in this study?

The addition of KRT-232 (AMG 232) to standard therapy of carfilzomib, lenalidomide, and dexamethasone is unlikely to help you. This study may help us learn things that may help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The 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.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

The study drug KRT-232 (AMG 232) will be supplied at no charge while you take part in this study. The cost of getting KRT-232 (AMG 232) ready and giving it to you *is also provided at no charge.* It is possible that the KRT-232 (AMG 232) may not continue to be supplied while you

are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of the other cancer drugs (carfilzomib, lenalidomide, and dexamethasone) that you will be treated with, tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. These include biopsies and blood draws that are being performed as part of routine standard of care testing from which research samples may also be obtained. However, you will not be responsible for the cost of research sample processing and research laboratory testing as this will be provided at no charge while you take part in this study. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor and any drug company supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

- Bone marrow aspirates and associated clinical laboratory data will be sent to Adaptive Biotechnologies (Seattle, WA) for genetic sequencing of your bone marrow aspirates for minimal residual disease detection (MRD).

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.

Who can answer my questions about this study?

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).*

ADDITIONAL STUDIES SECTION:
This section is about optional studies 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. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

For Optional Study #1 (Optional Bone Marrow Biopsy and Aspiration after Cycle 1 treatment) the results will be added to your medical records and you or your study doctor will know the results.

For Optional Study #2 (Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies), the results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say “no” to any or all of these studies. If you sign up for but cannot complete any of the 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 Studies

1. Optional Bone Marrow Biopsy and Aspiration after Cycle 1 treatment

If you agree, you will have a bone marrow biopsy and/or aspiration collected for additional testing after Cycle 1 of treatment to learn more about how the drug may work and what causes the drug to stop working in patients that initially respond to treatment.

You do not have to agree to take part in the optional procedures in order to be enrolled in this study.

WHAT IS INVOLVED?

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

1) A bone marrow biopsy and aspiration will be performed at the end of Cycle 1 treatment
2) To collect a bone marrow biopsy and aspirate, an area of the hip or other site is numbed with anesthetic and a small amount of bone marrow and bone is withdrawn through a large needle. The sample will be used for testing to evaluate for genetic changes to cells that may affect how the disease may react to the study drug and to evaluate for biomarkers in the blood and tissue that may be related to your reaction to the study drug.

WHAT ARE THE POSSIBLE RISKS?

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

WHAT ARE THE POSSIBLE BENEFITS?

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?

There are no costs to you for the optional procedures. The costs of the optional bone marrow biopsy will be covered by your insurance or the study.

You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

You may change your mind at any time to participate in the optional bone marrow biopsy and aspirations. If you decide you no longer to participate, please let your research team know or you can contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the optional bone marrow biopsy and aspiration, contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

Please circle your answer to show whether or not you would like to take part in each option. *(The sentence above can be deleted when consent is converted to the electronic form).*

Optional Procedure #1: Do you agree to have additional bone marrow sample collected to learn more about how the drug may work and what causes the drug to stop working in patients that initially respond to treatment?

YES NO

2. Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part, blood and left-over bone marrow material from your previous biopsies will be collected. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking”. The Biobank is being run by Experimental Therapeutics Clinical Trials Network (ETCTN) and supported by the National Cancer Institute. The samples will be physically stored at the University of Texas MD Anderson Cancer Center.

WHAT IS INVOLVED?

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

1) About 2 tablespoons of blood will be collected from a vein in your arm before you begin the study.

2) Left-over genetic material extracted from any bone marrow material from your bone marrow biopsies and aspirations performed while on the clinical study will be sent to the Biobank.
3) Your sample and some related health information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
4) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples unless your study doctor is directly participating in the research related to your samples.
6) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique 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.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that 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 researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.

2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and ETCTN staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom ETCTN sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

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?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

Please circle your answer to show whether or not you would like to take part in each option. *(The sentence above can be deleted when consent is converted to the electronic form).*

SAMPLES FOR THE LABORATORY STUDIES:

I agree to have my specimen collected and I agree that my specimen sample(s) and related information may be used for the laboratory study(ies) described above.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to learn about results from this(ese) study(ies).

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician 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 Main 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 copy of this form. I agree to take part in the main study and 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_____

Calendar of Additional Tests and Procedures

Study Title for Study Participants: Testing the addition of KRT-232 (AMG 232) to usual chemotherapy for relapsed multiple myeloma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10076. A Phase 1 Dose-Escalation and Exploratory Dose Expansion Study of KRT-232 (AMG 232) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone in Relapsed and/or Refractory Myeloma

Cycle (Each cycle = 28 days)	Pre-Cycle	Cycle 1			Cycle 2 and beyond	Post-Cycle
Clinic Visit Number	1	2	3	4	5+	To Be Determined
Visit Description	Screening	Exam and 1st dose	Exam	Exam	Exam	End of Treatment
Cycle Day(s)	-28 to 0	1	8	15	1	
Bone marrow aspiration and biopsy	X				X (O)	X
Blood sample for drug concentration measurement		X Collected once before 1st dose of KRT-232 (AMG 232) dose and at 1 hr, 3 hr, 5 hr, 8 hr, and 24 hr after 1st dose of KRT-232 (AMG 232)				
Blood samples for biomarker testing		X Collected pre-dose and 24 hr after 1st dose of KRT-232 (AMG 232)				
Blood sample for banking (O)	X				X	X
Myeloma bony survey	X					
Echocardiogram	X					
Buccal mucosal swab	X					

O - Optional