NRG-DT001 Consent Form

Study Title for Study Participants: Testing the Safety of Combining the Investigational Drug, AMG 232 (KRT-232), with Standard of Care Radiation Therapy Prior to Surgery in Soft Tissue Sarcoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: "NRG-DT001- A Phase IB Trial Of Neoadjuvant AMG 232 (KRT-232) Concurrent With Preoperative Radiotherapy In Wild-Type P53 Soft Tissue Sarcoma (STS)."

What is the usual approach to my soft tissue sarcoma?

You are being asked to take part in this research study because you have a type of cancer called soft tissue sarcoma. People who are not in a study are usually treated with radiation therapy followed by surgery to remove the tumor. Some patients also receive chemotherapy.

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
- 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 AMG 232 (KRT-232) given with radiation in patients with sarcoma prior to surgery. The AMG 232 (KRT-232) is investigational. It has been tested in other cancers but not yet in sarcoma. AMG 232 (KRT-232) has not been tested using the dosing schedule in this study and it has not been tested with radiation therapy. This study tests increasing frequency of AMG 232 (KRT-232) doses (2-5 per week) to determine the maximum safe dose, if any, that can be used in combination with radiation therapy. The dose that you receive will depend on when you begin to participate in this study. There will be between 12 to 46 people taking part in this study.

Based on animal studies, AMG 232 (KRT-232) is thought to activate a gene called p53 that can protect against cancer by triggering tumor cell death when the tumor cells are damaged by radiotherapy. Patients in this study will have their tumor tested for p53 from a prior biopsy sample. It takes about 2 weeks to find out the status of the p53 gene. Because we don't want to delay your treatment, you can start the study protocol before you find out about the p53 gene test result.

If your tumor tissue is p53 unchanged (called the wild type), you can continue the study protocol. Studies of AMG 232 (KRT-232) in animals have shown the investigational drug is only effective on tumors where p53 is unchanged, but information from patients is lacking. If the p53 gene in the tumor sample is changed or deleted,

you will stop the study drug and receive radiation alone, which is the usual treatment for this disease. We estimate that in 100 people with your cancer, 50 or fewer may have soft tissue sarcoma with the p53 gene that is changed or deleted.

What are the study groups?

All participants will receive AMG 232 (KRT-232) (the study drug) and the usual care radiation to the tumor prior to surgery.

Different total weekly dose of the study drug AMG 232 (KRT-232) will be given to several study participants. The first several participants will receive a dose that is determined safe based on other studies of AMG 232 (KRT-232) given alone without radiation. If the study drug in combination with radiation therapy does not cause serious side effects, it will be given to other study participants at a higher dose. The number of weekly doses will continue to increase for every group of study participants until side effects occur that require the dose to be lowered. Then the study will no longer accept new patients. The dose of the study drug you receive will depend on when you enter the study.

The study drug is taken by mouth on an empty stomach for a total of 6 weeks. Take AMG 232 (KRT-232) at least 2 hours after a meal and 2 hours before the next meal with a full glass (240 mL) of water. Take the tablets whole. Do not crush or dissolve in water. You will receive a Pill Diary that provides the instructions for taking the pills, the schedule, and to record taking the pills.

The study will evaluate two groups based on where the tumor is located.

Group A:
Participants in this group have sarcoma on their extremities (arms/legs) or body wall. Radiotherapy will be directed to this region as for the usual care.

Group B:
Participants in this group have sarcoma in the abdomen/pelvis or the “retroperitoneum” (a space behind our bowels). Radiotherapy will be directed to this region as for the usual care.

How long will I be in this study?

You will receive the study drug, AMG 232 (KRT-232) alone for 1 week and the study drug plus the usual radiation for 5 weeks, for a total of 6 weeks of treatment. If the p53 gene in the tumor sample is changed or deleted, you will stop the study drug but still receive 5 weeks of radiation (standard-of-care treatment).

Four weeks after end of radiation you will be evaluated by your study doctor for side effects. Surgical removal of the tumor will be scheduled for 5-8 weeks after you complete radiation.

After you finish the study drug and radiation, your doctor will continue to watch you for side effects and follow your condition with a clinical visit and appropriate imaging studies every 3 months for 2 years, then final follow-up at 2.5 years from end of radiation.

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 laboratory tests that you will need to have if you take part in this study.

Before you begin the study:

- You agree to release tissue from your previous biopsy. If there is not enough biopsy tissue to be tested you may not be able to participate in the study. Your study doctor may ask your permission to obtain another biopsy for clinical indications, such as to confirm the grade and type of sarcoma, and to test for the status of the p53 gene.
- You will be asked to provide the study doctor with list of herbs vitamins, and supplements (for your safety)
- Blood tests to monitor bleeding risk and liver function.

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 following extra tests. They are not part of the usual approach for your type of cancer.

During the study:

- Blood tests to monitor for side effects of the study drug.
- You agree to submit tumor tissue from the on-study surgery to assess response to treatment.
- Blood draws to measure the amount of AMG 232 (KRT-232) in your blood stream and to assess if the study drug is working in the cells. This is called pharmacokinetics (PK) and pharmacodynamics (PD) studies. A total of 13 blood draws will be needed. If you stop taking AMG 232 (KRT-232) because your p53 gene is changed or deleted, or for any other reason, the PK and PD blood draws will no longer be required.

A study calendar that shows the schedule of extra tests that will be done is attached.

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:

- 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.
- The study drug/study approach may not be better, and could possibly be worse, than the usual approach for your cancer, which is preoperative radiotherapy alone prior to surgery.
- 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.
- 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 are laws against misuse

of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

- There can also be a risk in finding out new genetic information about you. It is possible, though unlikely, that examination of your DNA in this study could uncover a mutation that you have inherited from one or both of your parents. Such a mutation might have significance for your health or that of your blood relatives. If a mutation is found, the information can be sent to your doctor and your doctor will discuss the results with you. It might be recommended that you meet with a genetic counselor to discuss the meaning of this mutation and whether further evaluation is needed. This type of follow up is considered usual care and is not part of this study. Patients who have inherited p53 mutations--a condition called Li-Fraumeni syndrome--will most likely have p53-mutant tumors and will therefore be unable to remain in the study. The finding of an inherited mutation (other than within the p53 gene) will not affect your eligibility to receive AMG 232 (KRT-232) in this study. If you do not wish to be told about any inherited mutations, you may say so and that information will not be sent to your doctor.

  Please choose your answer to following questions.

  I choose to be told about inherited mutations that are uncovered in my DNA during this study.

  YES NO

  If you choose NO, indicating that you do not want to be told about inherited mutations, do you want your study doctor to receive information about inherited mutations uncovered in this study?

  YES NO

The radiation therapy and AMG 232 (KRT-232) (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 be testing your blood and will let you know if changes occur that may affect your health.

You will receive radiotherapy as part of the standard treatment of soft tissue sarcoma. Specific side effects from radiotherapy will depend on the location of your cancer, and discussed below. It is possible that combining AMG 232 (KRT-232) with radiation therapy may increase the side effects of radiation therapy or AMG 232 (KRT-232) depending on the location of the tumor.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- The study doctors do not know how common or serious the side effects from the combination of the drug and radiation therapy will be.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.

- The study doctor may be able to treat some side effects.
- The 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 that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

You will receive a study drug information handout and wallet card to help you avoid medications and/or herbal supplements that may interact with the study drug and with your doctor's contact information so you may promptly notify your doctor of any changes (See Appendix I).

Study Groups A and B: Possible Side Effects for AMG 232 (KRT-232) (Table Version Date: December 22, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving KRT-232 (AMG 232**)**, more than 20 and up to 100 may have:
• Diarrhea, nausea, vomiting • Bruising, bleeding • Loss of appetite

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving KRT-232 (AMG 232), from 4 to 20 may have:
• Anemia which may require blood transfusion • Pain • Swelling of arms, legs • Tiredness • Changes in taste

Diarrhea is a common side effect of the study drug and can be managed taking the anti-diarrhea medication, loperamide. You study doctor will instruct you how to take anti-diarrhea medication either before or when this side effect occurs.

Study Group A: Possible Side Effects of Extremity/Body Wall Radiation

Early Radiation therapy reactions: up to 90 days from start of treatment:

COMMON, SOME MAY BE SERIOUS In 100 people receiving extremity/body wall radiation, more than 20 and up to 100 may have:

• Skin redness, peeling, blisters on the skin
• Tiredness
• Anemia which may require transfusion
• Infection, especially when white blood cell count is low
• Bruising, bleeding
• If abdomen or pelvis is in the treatment area:
  o Irritation of the rectum causing painful or urgent bowel movements
  o Need to urinate more often than usual, pain with urination

COMMON, SOME MAY BE SERIOUS In 100 people receiving extremity/body wall radiation, more than 20 and up to 100 may have:
o Nausea, vomiting, diarrhea • Non-healing surgical site

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving extremity/body wall radiation, from 4 to 20 may have:
• If the lung is in the treatment area: shortness of breath, cough

Late radiation therapy reactions: greater than 90 days after start of treatment:

COMMON, SOME MAY BE SERIOUS In 100 people receiving extremity/body wall radiation, more than 20 and up to 100 may have:
• Dry skin, darkening of the skin, which may be permanent • Scarring or thickening of soft tissue • Delayed wound healing • Hair loss, which may be permanent

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving extremity/body wall radiation, from 4 to 20 may have:
• Broken bone • Joint stiffness • Swelling of the treated arm or leg • Pain

RARE, AND SERIOUS In 100 people receiving extremity/body wall radiation, 3 or fewer may have:
• Damage to the spinal cord and nerves, which may cause muscle weakness, muscle contraction, loss of muscle function, numbness, paralysis, and inability to control bowel movements and/or urine • Damage to blood vessels, which may cause swelling, pain • Kidney damage which may cause swelling, may require dialysis • If the following organs are in the treatment area, scarring can damage these organs: o Heart: dizziness, weakness, shortness of breath, chest pressure pain, and/or abnormal heart beat o Lung: scarring of the lungs which may cause shortness of breath, may be permanent o Abdomen or Pelvis: sores in the internal organs, blockage of the internal organs which may cause pain, vomiting, or inability to pass stools o Reproductive organs: infertility (inability to father children or become pregnant) • A new cancer in the tissue that received radiation

Study Group B: Possible Side Effects of Abdominal/Retroperitoneal Radiation

Early radiation therapy reactions: up to 90 days from start of treatment:

COMMON, SOME MAY BE SERIOUS In 100 people receiving stomach/back radiation, more than 20 and up to 100 may have:
• Skin redness, peeling, or blisters on the skin • Tiredness • Anemia which may require transfusion • Bruising, bleeding • Infection, especially when white blood cell count is low • Nausea, Vomiting, Diarrhea • Weight loss

Late radiation therapy reactions: greater than 90 days after start of treatment:

COMMON, SOME MAY BE SERIOUS In 100 people receiving stomach/back radiation, more than 20 and up to 100 may have:
• Dry skin, darkening of the skin, which may be permanent • Scarring or thickening of soft tissue • Hair loss, which may be permanent

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving stomach/back radiation, from 4 to 20 may have:
• A tear or hole in the internal organs which may cause belly pain or that may require surgery • Blockage of the internal organs which may cause pain, vomiting, or may require surgery • Infertility (inability to father children or become pregnant)

RARE, AND SERIOUS In 100 people receiving stomach/back radiation, 3 or fewer may have:
• Damage to the spinal cord and nerves, which may cause muscle weakness, muscle contraction, loss of muscle function, numbness, paralysis, and inability to control bowel movements and/or urine • Damage to blood vessels, which may cause swelling, pain • Liver damage, which may cause yellowing of the eyes and skin, swelling • Kidney damage which may cause swelling, may require dialysis • A new cancer resulting from treatment of earlier cancer

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.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The radiation therapy and study drug therapy 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. Pregnancy

prevention must continue for 12 months after the study medication is stopped. Please notify your study team immediately if you find out you are pregnant.

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

It is not possible to know at this time if the study approach is better than the usual approach, so this study may or may not 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 Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

What are the costs of taking part in this study?

The study drug will be supplied at no charge while you take part in this study. The cost of getting the study drug ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that the study drug 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.

Neither you nor your health plan/insurance company will be billed for the tests on your tumor tissue and the PK/PD blood draws.

You and/or your health plan/insurance company will need to pay for all of the other costs of caring for your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. 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. Contact information for your study doctor is listed on the consent cover page. 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.

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.
There are organizations that look at or receive copies of the information in your study records. These organizations are required to make sure your information is kept private, unless required by law to give it to another group. Some of these organizations are:

- Montana Cancer Consortium
- NRG Oncology and Amgen, or any drug company supporting the study;
- Other organizations in the National Clinical Trials Network (NCTN): Imaging and Radiation Oncology Core (IROC).
- The NCI Central 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 (FDA) and the groups it works with to review research.
- The NCI and the groups it works with to review research, including the Cancer Trials Support Unit (CTSU).

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

ADDITIONAL STUDIES SECTION:

This part of the consent form is about an optional study that you can choose to take part in. You will not get health benefits from this study. 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.

You will not be billed for this optional study. You can still take part in the main study even if you say 'no' to this study. If you sign up for but cannot complete the study for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for the following study.

Optional Sample Collection for Laboratory Tissue Study

If you choose to take part in this optional study: If you undergo a biopsy because your tumor progresses or returns while you are on the main study or a second tumor occurs in the same area, the study doctor from the main study would like to collect the tumor tissue to assess changes in the tumor and/or confirm the diagnosis.

WHAT IS INVOLVED IN THE LABORATORY TISSUE STUDY?

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

1) Your sample and some related health information will be sent to a researcher for use in the study described above.
2) 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.
3) 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 OF THE LABORATORY TISSUE STUDY?

1) 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.
2) 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.
3) 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 laboratory tissue study 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 is sent to the study 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 you will be kept separate from your sample and health information. Any NRG Oncology staff with access to the list must sign an agreement to keep your identity confidential.
3) The study researchers to whom NRG Oncology 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 in the laboratory tissue study.

The study researchers, using the sample 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 call the study doctor, who will let the study researchers know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains 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 study 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. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR THE LABORATORY TISSUE STUDY:
I agree to have my specimen collected and I agree that my specimen sample and related information may be used for the laboratory study 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 study.

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 Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)

Study Calendar

	Procedure or Patient Activity
Before the study	
Baseline tests	Following your voluntary **consent** to take part: • Tumor sample submission from archive (prior diagnostic sample) for p53 gene testing • Baseline blood tests to check bleeding risk and liver function.
During the study	
Lead-in part 1 Week before receiving radiotherapy	• AMG 232 (KRT-232) by mouth see Pill Diary for instructions, schedule, and to record taking it. • Research blood tests: Before dose of study drug, then 1, 3, 5, 8, and 24 hours after study drug • Blood test to check bleeding risk and liver function
Week 1 during Radiation Therapy	• AMG 232 (KRT-232) pill by mouth see Pill Diary for instructions, schedule, and to record taking it. • Blood test to check bleeding risk and liver function • Research blood tests: Before dose of study drug, then 24 hours after study drug
Week 2 during Radiation Therapy	• AMG 232 (KRT-232) pill by mouth see Pill Diary for instructions, schedule, and to record taking it.

	• Blood test to check bleeding risk and liver function
Week 3 during Radiation Therapy	• AMG 232 (KRT-232) pill by mouth see Pill Diary for instructions, schedule, and to record taking it. • Research blood tests: Before dose of study drug, then 24 hours after study drug • Blood test to check bleeding risk and liver function
Week 4 during Radiation Therapy	• AMG 232 (KRT-232) pill by mouth see Study Drug Diary for details, schedule, and to record taking it. • Blood test to check bleeding risk and liver function
Week 5 during Radiation Therapy	• AMG 232 (KRT-232) pill by mouth see Pill Diary for instructions, schedule, and to record taking it. • Research blood tests: Before dose of study drug, then 24 hours after study drug • Blood test to check bleeding risk and liver function
4 to 8 weeks after completion of the AMG 232 (KRT-232) and radiotherapy	• Surgery to remove tumor (5 to 8 weeks after AMG 232 (KRT-232) and radiation treatment) • Send tumor tissue from surgery

Appendix I: PATIENT DRUG INTERACTIONS HANDOUT AND WALLET CARD

Information for Patients, Their Caregivers and Non-Study Healthcare Team on Possible Interactions with Other Drugs and Herbal Supplements

Patient Name:		**Diagnosis:**		**Trial #:**	
Study Doctor:		**Study Doctor Phone #:**		**Study Drug(s):**	**AMG 232 (KRT-232)**

Please show this paper to all your healthcare providers (doctors, physician assistants, nurse practitioners, pharmacists), and tell them you are taking part in a clinical trial sponsored by the National Cancer Institute.

These are the things that your healthcare providers need to know:

AMG 232 (KRT-232) interacts with certain specific liver enzymes and certain transport proteins that help move drugs in and out of cells. AMG 232 (KRT-232) may also interact with certain stomach acid-reducing medications.

	Explanation
CYP Isoenzymes	The enzymes in question are CYP3A4 and CYP2C8. AMG 232 (KRT-232) is a moderate inhibitor of CYP3A4 and CYP2C8 and also induces CYP3A4 and may effect other drugs that are metabolized by these enzymes.
Glucuronidation	AMG 232 (KRT-232) is metabolized by UGT1A1, UGT1A3, and UGT1A4 and is a moderate inhibitor of UGT1A1. AMG 232 (KRT-232) may be affected by other drugs that inhibit or induce these enzymes and may affect other drugs that are metabolized by UGT1A1.
Transport Proteins	The protein in question is P-gp. AMG 232 (KRT-232) is a substrate of P-gp and may be affected by other drugs that inhibit or induce this transport protein.
Acid reducing medications	Antacids and drugs known as proton-pump inhibitors may reduce the effectiveness of AMG 232 (KRT-232).

These are the things that you need to know:

The study drug AMG 232 (KRT-232), may interact with other drugs which can cause side effects. For this reason, it is very important to tell your doctors about all your medicines, including: (a) medicines you are taking before this clinical trial, (b) medicines you start or stop taking during this clinical trial, (c) medicines you buy without a prescription (over-the-counter remedy), (d) herbals or supplements (e.g. St. John's Wort). It is helpful to bring your medication bottles or an updated medication list with you.

Before you enroll onto the clinical trial, your study doctor will work with your regular health care providers to review any medicines and herbal supplements that are considered substrates of CYP3A4 and CYP2C8 or inhibitors or inducers of transport protein P-gp. certain medicines used to reduce stomach acid.

- Please be very careful! Over-the-counter drugs (including herbal supplements) may contain ingredients that could interact with your study drug. Speak to your doctors or pharmacist to determine if there could be any side effects.
    - Use caution when taking antacid and over-the-counter stomach acid reducing medicines called proton pump inhibitors. Examples of proton pump inhibitors include Prilosec, Prevacid and Nexium. Discuss with your study team if you can take them.

- Make sure your doctor knows to avoid certain prescription medicines.
    - Avoid any medicines considered substrates of CYP3A4 and CYP2C8.
    - Avoid any medicines considered inhibitors or inducers of P-gp.
    - Avoid any medications considered inhibitors or substrates of UGT1A1.
    - Use caution when taking antacids or prescription medicines called proton pump inhibitors.

- Your regular health care provider should check a frequently updated medical reference or call your study doctor before prescribing any new medicine or discontinuing any medicine.

(Next page: Patient Drug Interaction Wallet Card)

Patient Drug Interaction Wallet Card

NIH NATIONAL CANCER INSTITUTE EMERGENCY INFORMATION	NIH NATIONAL CANCER INSTITUTE	NIH NATIONAL CANCER INSTITUTE DRUG INTERACTIONS	NIH NATIONAL CANCER INSTITUTE
Show this card to all of your healthcare providers. Keep it with you in case you go to the emergency room.	Tell your doctors **before** you **start** or **stop** any medicines. **Check with your doctor or pharmacist if you need to use an over-the-counter medicine or herbal supplement!**	**Carry this card with you at all times** **AMG 232 (KRT-232)** interacts with certain specific liver enzymes and certain transport proteins that help move drugs in and out of cells and must be used very carefully with other medicines.	
Patient Name: **Diagnosis:** **Study Doctor:** **Study Doctor Phone #:** **NCI Trial #:** **Study Drug(S): AMG 232 (KRT-232)**	**Use caution and avoid the following drugs if possible:**	Your healthcare providers should be aware of any medicines that are substrates of CYP3A4, CYP2C8 or UGT1A1; inhibitors or inducers of transport protein P-gp; and any medicines that are considered inhibitors of UGT1A1; certain medicines used to reduce stomach acid. **Before prescribing new medicines**, your health care provider should check a **frequently-updated medical reference** for a **list of drugs to avoid** or contact your study doctor. Version May 2019	
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