THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase Ib/II study of grapiprant (IK-007) and eribulin combination treatment for metastatic inflammatory breast cancer (mIBC)
2021-0077

Subtitle: IK-007

Study Chair: Sadia Saleem

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn about the safety and effects of the combination of 2 different study drugs, grapiprant (also called IK-007) and eribulin, when given to patients with metastatic inflammatory breast cancer (mIBC). Metastatic means it has spread to other parts of the body.

This is an investigational study. Grapiprant is not FDA approved or commercially available. It is currently being used for research purposes only. Eribulin is FDA approved and commercially available for the treatment of mIBC. It is considered investigational to give eribulin and grapiprant together to treat mIBC.

The study doctor can explain how the study drugs are designed to work.

The study drugs may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

You may receive the study drugs until the disease gets worse or the study doctor thinks that it is no longer in your best interest. After that, you will be in follow-up for up 5 years. You will no longer be able to take the study drugs if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Grapiprant will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the costs of eribulin.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard chemotherapy, hormonal therapy, targeted therapy, or combination of these drugs if appropriate. The study doctor will discuss the possible risks and benefits of these treatments. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- You will have an EKG and either a MUGA scan or an echocardiogram (ECHO) to check your heart function.
- Blood (about 5 tablespoons) will be drawn for routine tests and for future biomarker research related to this study. Biomarkers are found in the blood/tissue/urine and may be related to your reaction to the study drugs.
- Urine will be collected for routine and biomarker testing.
- You will have imaging scans (chest x-ray, PET/CT, CT, MRI, mammogram, ultrasound, and/or bone scan) to check the status of the disease. The study doctor will tell you which imaging scans you may have.
- You will have a biopsy to collect tumor samples for biomarker testing. The study doctor will tell you what kind of biopsy you will have.
- If you can become pregnant, part of the above blood or urine sample will be used for a pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be enrolled in 1 of 2 study groups (Group 1 or Group 2) based on when you enroll in the study. Group 2 will begin enrollment after Group 1 is complete.

All participants will receive the same drugs at the same schedule, and the same dose of eribulin. However, Group 1 may receive 1 of 2 different doses level of grapiprant depending when they enroll in the study. The study doctor will tell you what dose of grapiprant you are receiving.

Up to 25 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each cycle is 21 days.

You will receive **eribulin** by vein over about 5 minutes on Days 1 and 8 of each cycle.

You will take **grapiprant** by mouth 2 times every day or as instructed by your doctor with food or within 2 hours after eating. You should take your doses at about the same time every day. You should swallow the tablets whole with about a cup (8 ounces) of water. Do not chew, crush, or break the tablets.

If you vomit a dose, do not take a replacement or “make up” dose. Wait and take your next dose as scheduled.

If you are in Group 2, you will have a 14-day “pre-cycle” before the start of Cycle 1 in which you will take grapiprant alone for 2 weeks. After the pre-cycle, you will begin taking both study drugs.

Study Visits

On Day 1 of each cycle:

- You will have a physical exam.
- Blood (about 1 tablespoon) will be drawn for routine tests.
- You will have an EKG, if your doctor thinks it is needed.

On **Day 8 of each cycle,** blood (about 1 tablespoon) will be drawn for routine tests.

Before **Cycle 2 (Group 1) or after the pre-cycle, but before the start of Cycle 1 (Group 2):**

- Blood (about 2 tablespoons) will be drawn for future research.
- Urine will be collected for biomarker testing.
- You will have a core biopsy to collect tumor tissue for immune system and genetic testing, which may help researchers understand how the study drugs work in your body.

Before **Cycle 3 and then every 3 cycles after that** (Cycles 6, 9, 12, and so on), you will have imaging scans to check the status of the disease.

End-of-Treatment Visit
Within about 7 days after your last dose of study drugs:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.
- You will have imaging scans, if you have not had one in the last 3 cycles or if the doctor thinks you need one.

Follow-Up
About 30 days after your last dose of study drugs, and then 1 time every year after that for up to 5 years, you may be contacted (either by phone or in-person during an already-scheduled clinic visit) and asked about how you are doing and if you have started any new anti-cancer medications. If you are called, each call should last about 2-5 minutes. The study staff may also review your electronic medical record every year for up to 5 years.

Other Information
While on you are on study, there are certain foods and drugs you should avoid. For example, avoid having any grapefruit and products containing grapefruit juice.

It is very important that you tell the study doctor about any drugs you are taking or plan to take, including prescription and over-the-counter drugs, herbal supplements or remedies, corticosteroids, or vitamins/supplements.

You cannot receive any live vaccine (such as FluMist®) within 30 days before your first dose of grapiprant and while on study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Grapiprant Side Effects

This is an early study of grapiprant, so the side effects are not well known.
Based on early human studies, grapiprant may cause:

• high blood pressure • fast/irregular heartbeat • high blood levels of sodium (possible weakness and/or swelling)	• abdominal pain vomiting • inflammation of the intestines • stomach ulcers (sores) • diarrhea	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • abnormal kidney tests (possible kidney damage)

Eribulin Side Effects

Common (occurring in more than 20% of patients)

• fatigue • fever • hair loss (partial or total) • nausea	• constipation • weight loss • weakness • pain	• nerve damage (possible numbness, pain, and/or loss of motor function)

Eribulin may commonly cause low blood cell counts (red blood cells and white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Occasional (occurring in 3-20% of patients)

• headache • loss of appetite • diarrhea	• vomiting • abnormal liver tests (possible liver damage)	• difficulty breathing • cough

Exact frequency unknown but occurring in fewer than 10% of patients:

• swelling (arm/leg) • depression • dizziness • difficulty sleeping • skin rash	• low blood levels of potassium (possible weakness and/or muscle cramps) • mouth blisters/sores (possible difficulty swallowing)	• abdominal pain • upset stomach • abnormal taste • dry mouth • muscle spasms • teary eyes • infection

Rare but serious (occurring in fewer than 3% of patients)

• abnormal EKG • low blood levels of magnesium (possible weakness, muscle cramps, and/or irregular heartbeat) • inflammation of the pancreas (possible abdominal pain)	• dehydration • low platelet count • liver damage • lung inflammation (possible difficulty breathing)	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • allergic reaction

Eribulin may rarely cause a low platelet cell count. A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

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.

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

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

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A **PET scan** may cause you to feel "closed in" while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

X-rays send a small amount of radiation though the body. All radiation adds up over a lifetime and may increase the risk of a new cancer forming.

A **standard bone scan** exposes you only to the radiation that comes from injecting the standard radioactive imaging solution for bone imaging.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study.

If you can become pregnant or father a child and you are sexually active, you must use birth control during the study and at least 6 months after your last dose of study drugs. Effective methods of birth control include:

- Use of hormonal birth control methods: pills, shots/injections, implants (placed under the skin by a health care provider), or patches (placed on the skin)
- Intrauterine devices (IUDs)
- Using 2 barrier methods (each partner must use 1 barrier method) with

spermicide. Males must use a male condom (latex or other synthetic material) with spermicide. Females must choose either a diaphragm with spermicide, or cervical cap with spermicide, or a sponge.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or IKENA Oncology for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You may receive some reimbursement for costs that are a direct result of your participation, such as travel expenses. You may receive up to a maximum of $100 for hotel costs per visit (up to 6 times), you may receive up to a maximum of $15 for parking per visit (up to 6 times), for a total amount of up to $600.You will need to provide receipts for your expenses to be eligible for reimbursement. Please ask the study staff about this possible reimbursement.

Additional Information

4. You may ask the study chair (Dr. Sadia Saleem, at 281-566-1900) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, IKENA Oncology, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, including the results of all of your standard tests performed as part of this research, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: IKENA Oncology.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and IKENA Oncology, and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as urine, blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. IKENA Oncology and Labcorp will not store leftover samples for future research.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples

Genetic Research
Samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s). However, your first cycle (Cycle 1 Day 1) of treatment must be given at MD Anderson.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - IKENA Oncology, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Labcorp, a laboratory for the urine test for this study
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected. If you

withdraw from the study, the study staff may ask if they can continue collecting the results of routine care from your medical record.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2021-0077

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION