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Study Title: A Phase 1 Open Label Study of KPT-9274 in Patients with Relapsed or Refractory Acute Myeloid Leukemia

Key Information

Please read all the information below and ask questions about anything you don't understand before deciding if you want to take part.

You are being asked to be in a research study. Participation in Research is voluntary.

Purpose of the Study: We are doing this study to learn more about how KPT-9274 (the study drug) may treat your type of cancer. This study drug has not been FDA approved, and is therefore considered investigational.

Procedures: If you agree to participate, the following will happen:

- You will have a screening visit to make sure you are eligible to be in the study. This will include a bone marrow biopsy.
- If you are eligible and agree to participate, you will visit the study doctor during each 28 day cycle (more detail provided in the treatment phase section). You will participate in at least one cycle.
- You will have a bone marrow biopsy twice during the first cycle, and periodically thereafter.
- You will remain on study for one year after treatment ends.

Risks: Participation in research involves risks, including the following:

- Risks associated with KPT-9274 include: anemia; joint pain and/or swelling; extreme tiredness; muscle pain; digestive problems; liver enzyme increase; shortness of breath; decreased appetite; skin problems; back pain; dizziness, increased heart rate; changes to liver and pancreatic enzymes, potassium, magnesium, sodium, blood sugar increase, albumin, blood platelets; insomnia; urine protein increase; swelling in feet and legs; fever; weight loss; influenza-like illness.

- Risks associated with bone marrow biopsy: A bone marrow biopsy may result in bleeding, infection, local nerve damage, pain from the needle sticks, and pain from aspirating the bone marrow with a syringe.

Benefits: There is no guarantee that your health will improve if you join this study. This study may lead to information that could help patients and health care providers in the future.

Alternatives: There may be other ways of treating your type of cancer. Please discuss other treatment options with your doctor.

Detailed Consent

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?

This study plans to learn more about a new drug and how well the drug works to treat your type of cancer. The drug being used in this study is KPT-9274. This study will be looking at how safe, effective, and tolerable KPT-9274 is when used with patients with relapsed or refractory acute myeloid leukemia. KPT-9274 is considered investigational. "Investigational" means that the study drug has not been approved by U.S Food and Drug Administration (FDA).

You are being asked to be in this research study because you have relapsed or refractory acute myeloid leukemia (AML). This study is the first time that KPT-9274 is being tested for patients with AML. AML is a cancer, and cancers are uncontrolled growths of cells. Cancer cells can only maintain uncontrollable growth through increased energy production and consumption. The study drug KPT-9274 is designed to work by inhibiting proteins that are required for cancer cells to produce energy and multiply thus stopping cancer cell growth or causing cancer cell death. It is not known if KPT-9274 will treat your cancer.

KPT-9274 may be referred to as the "study drug" during this consent form.

Other people in this study

Up to 40 people from your local area and country will participate in the study.

What happens if I join this study?

If you join the study, you will be asked to sign this consent form. You will be given a copy to keep and the original form will be kept at the clinic. You can withdraw from the study at any time and without giving a reason and this will not affect the standard medical care you receive.

While you are taking part in this study, some of the tests and procedures are the same type that would be performed as part of your regular cancer care even if you did not join the study. Some of the tests and procedures are required only for the study.

The first tests and procedures will be done to see if you are eligible to join this study. You may have had some of these tests and procedures done recently as standard care for your cancer, and they may not need to be repeated. Please speak with your study doctor about your study treatment duration.

This study has three periods:
1) Screening
2) Treatment
3) Post-treatment

Screening Phase (within 30 days before treatment)

- Informed Consent
- Review of medical history and demographics
- Physical exam, including weight, height, and vital signs.
- Blood draw for routine tests
- Pregnancy test for women of child-bearing age (blood or urine)
- Counseling on the risks of pregnancy while in this study
- Bone marrow aspiration and biopsy
- Electrocardiogram (EKG)

After screening is completed and the study doctor agrees that you can continue with the study, you will begin the study treatment. Each cycle is 28 days long and there is a minimum of one cycle on this study.

Treatment phase

During Cycle 1 you will receive three doses of the study drug per week, which totals to 12 doses in a 28-day period.

The use of niacin or niacin-containing supplements, including multivitamins and energy drinks is not allowed while you are taking the study drug.

Cycle 1 Day 1
- Examination, vital signs, bloodwork, and ECG
- 1st dose of the study drug

Cycle 1 Day 2
- Bloodwork

Cycle 1 Day 3 and 5
- 2nd and 3rd dose of the study drug

Cycle 1 Day 8
- Examination, vital signs, and bloodwork
- Bone marrow biopsy
- 4th dose of the study drug

Cycle 1 Day 10 and 12
- 5th and 6th doses of the study drug

Cycle 1 Day 15
- Examination, vital signs, and bloodwork
- 7th dose of the study drug

Cycle 1 Day 17 and 19
- 8th and 9th doses of the study drug

Cycle 1 Day 22
- Examination, vital signs, and bloodwork

- 10th dose of the study drug

Cycle 1 Day 24 and 26
- 11th and 12th doses of the study drug

Cycle 1 Day 28
- Bone marrow biopsy

There is the possibility of adding additional cycles to your treatment with a higher dose of the study drug. Your Study Doctor will evaluate where you have met the criteria for dose expansion cycles once you completed all 28 days of Cycle 1.

Cycle 2 Day 1
- Examination, vital signs, bloodwork, and ECG

Cycle 2 Day 15
- Examination, vital signs, and bloodwork

Cycle 2 Day 28
- Bone marrow biopsy (as directed by Study Doctor)

Additional Cycles Day 1
- Examination, vital signs, bloodwork, and ECG

Additional Cycles Day 28
- Bone marrow biopsy (as directed by Study Doctor)

Your Study Doctor may adjust your study drug dosage during the trial. Your Study Doctor will discuss any changes with you.

Post treatment

After the end of treatment visit (EOT), there will be a safety follow-up visit 30 day later. Follow-up visits will continue every 3 months for a year after the safety follow-up.

What are the possible discomforts or risks?

Risks from the Study Drug

Discomfort you may experience while in this study include all the side effects associated with the study drug KPT-9274. Participation in a study necessarily carries risks. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Other drugs may be given to make side effects less serious and more tolerable (such as for nausea or diarrhea). Some risks described in this consent form may cause death.

The study drug KPT-9274 has been used in 60 human patients to date. Based on preliminary safety data from these 60 patients, and potential risks based on animal studies and other drugs in the same class of this drug, the risks and side effects are listed here:

The use of niacin or niacin-containing supplements (e.g., multivitamins and energy drinks) is not allowed while you are taking KPT-9274.

The following common side effects occurred in more than 10% of patients

- Anemia (low red blood cells)
- Fatigue (extreme tiredness)
- Arthralgia (joint pain and/or swelling)
- Nausea
- Difficult or labored breathing
- Diarrhea
- Vomiting
- Myalgia (muscle pain)
- Decreased appetite
- Flushing
- Liver enzyme increase (could be a sign of liver injury)
- Abdominal pain
- Small intestinal obstruction (which can be serious)

Other side effects

- Shortness of breath
- Pruritus (rash or itching)
- Back pain
- Dizziness
- Tachycardia (increased heart rate, more than 100 beats per minute)
- Constipation
- Lipase increase (could be a sign of pancreas injury)
- Decrease of blood potassium (might cause fatigue, constipation, or muscle weakness)
- Decrease of blood magnesium (might cause muscle weakness, numbness, or tremor)
- Decrease of blood sodium (might cause nausea, headache, confusion, or fatigue)
- Insomnia (difficulty falling asleep might result in daytime drowsiness)
- Proteinuria (urine protein increase, could be a sign of kidney injury)
- Blood sugar increase
- Blood albumin decrease
- Peripheral edema (swelling due to fluid usually in limbs such as feet and legs)
- Fever
- Weight decrease
- Influenza-like illness
- Blood in stools
- Thrombocytopenia (low platelets)

Other possible risk include:

Contraception and Pregnancy

It is unknown whether KPT-9274 might have reproductive toxicity in humans; therefore, all patients in this study must agree to use at least two forms of effective contraception during the study, and for 3 months after their last dose of KPT-9274.

Women who are pregnant or nursing a child cannot participate in this study. To participate in the study you must confirm, to the best of your knowledge, that you are not now pregnant, and that you do not intend to become pregnant during the study.

Although some women participating in this study can become pregnant, as a female participant in the study it is important that you use dual methods of contraception, including one highly effective, and one effective form of birth control method (contraception) during study treatment and for 3 months after your last dose, if you are sexually active and have a chance that you may become pregnant. Examples of highly effective and effective birth control methods are:

- Highly effective methods include:
  - Hormonal contraceptives (e.g. combined oral contraceptives, patch, vaginal ring, injectables, and implants)
  - Intrauterine device (IUD) or intrauterine system (IUS)
  - Vasectomy and tubal ligation
- Effective methods include:
  - Barrier methods of contraception (e.g., male condom, female condom, cervical cap, diaphragm, contraceptive sponge)
    Notes:
    - *No barrier method by itself achieves a highly effective standard of contraception*
    - *The proper use of diaphragm or cervical cap includes use of spermicide and is considered one barrier method.*
    - *The cervical cap and contraceptive sponge are less effective in parous women.*
    - *The use of spermicide alone is not considered a suitable barrier method for contraception.*
    - *When used consistently and correctly, "double barrier" methods of contraception (e.g., male condom with diaphragm, male condom with cervical cap) can be used as an effective alternative to the highly effective contraception methods described above.*
    - *Male and female condoms should not be used together as they can tear or become damaged.*

Acceptable methods of contraception also include:

- A sexual partner who is surgically sterilized or post-menopausal.
- Total abstinence. Periodic abstinence like calendar, ovulation, symptom-thermal, post-ovulation methods, and withdrawal are not acceptable methods of contraception for purpose of this Study.

Should you become pregnant during the course of the clinical trial, or suspect that you may be pregnant, you must inform your doctor immediately. You must also inform your doctor if you become pregnant within six months of the end of study treatment.

Fertile female patents must agree to refrain from egg donation from first dose of study treatment until at least 3 months following your last dose.

Men who take part in this clinical trial must use two highly effective methods of contraception to ensure that their female partners do not become pregnant either during the trial or within a period of 3.5 months after the end of study treatment because cancer treatment may lead to deformities

in the fetus. Should your partner become pregnant during the trial or within a period of 3 months of the end of study treatment despite using adequate methods of contraception, it is essential that you inform your doctor. Men are prohibited from sperm donation during the trial or within a period of 3.5 months after the end of study treatment.

Risks Associated with Procedures

Blood Taken (drawn)
In this study we will need to get about between 3-10 teaspoons of blood from you in a visit. We will get blood by putting a needle into one of your veins and letting the blood flow into a tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.

IV Inserted in Your Vein
In this study, we may insert a needle, connected to a plastic tube, into a vein. We will use the tube to take blood samples or give you fluids. You will feel some pain when we first insert the tube into your vein. You may have some redness, swelling, or bruising where the tube goes under your skin. In some cases, this type of tube can cause an infection where it goes under the skin. In rare cases, it can cause a blood clot in the vein. You will have this tube inserted for up to 12-24 hours.

Bone Marrow Aspirate / Biopsy
The risks of this procedure are small and include bleeding, infection, local nerve damage, pain from the needle sticks, and pain from aspirating the bone marrow with a syringe. This study may require that two biopsy cores are collected. The additional risk of the second biopsy core is minimal, though you may experience additional discomfort when the second biopsy core is obtained. Care will be taken to avoid these complications.

Electrocardiogram (ECG)
ECG is a noninvasive test of the impulses in your heart. You may have itching or bruising of the skin where the machine patches are placed for the ECG.

The study may include risks that are unknown at this time.

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

What are the possible benefits of the study?

This study is designed for the researcher to learn more about your cancer and the effects of the study drug on your cancer.

This study is not designed to treat any illness or to improve your health.

Are there alternative treatments?

There may be other ways of treating your cancer. These other ways include:

- Get treatment or care for your cancer without being in a clinical trial
- Taking part in another clinical trial

You have the following choices available to you:

- Get any of the cancer treatments listed above, together with a treatment for your pain and symptoms.
- Get treatment only for your pain and symptoms, but no treatment for the cancer itself.
- Get no treatment at all.

You should talk to your doctor about your choices. Make sure that you understand all of your choices before you decide to take part in the study. You may leave this study and still have these other choices available to you.

Who is paying for this study?

Karyopharm is providing funding support for this study. Karyopharm manufactures the study drug, KPT-9274, and will provide this drug for the study. This research is being conducted by Dr. Daniel Pollyea. The research study will only pay for procedures not considered standard of care, for this study most ECG will be paid by the research study. Your standard bone marrow biopsies or aspirates will be billed to your insurance.

Will I be paid for being in the study?

You will not be paid to be in the study.

Will I have to pay for anything?

You will not be charged for the study drugs that you receive as part of this study. Your health care insurance will be charged for test/procedures required for your normal standard of care. You will not receive payment for participating in this sponsor-investigator research.

The other study drug regimens are considered standard treatment for your type of cancer. These drugs will be obtained through your insurance, and you will be responsible for any applicable copays required by your insurance policy.

There are some medical procedures that you would get for your condition whether you were in this study or not, such as routine blood draws, imaging, drugs for standard of care regimens, and administration. These are considered standard of care. You and/or your health insurance may be billed for the costs of medical care during this study, if these expenses are related to standard of care procedures. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs, or you do not have insurance, these costs will be your responsibility.

Ask your study doctor to discuss the costs that will or will not be covered by this research study. This discussion should include the costs of treating possible side effect. Otherwise, you might have unexpected expenses from being in this study.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time.

What happens if I am injured or hurt during the study?

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care. The sponsor and the investigator will determine if your injury or illness is research-related. The term "research-related injury" means physical injury caused by drugs or procedures required by the study which are different from the medical treatment you would have received if you had not participated in the trial.

If you have an injury while you are in this study, you should call Dr. Daniel Pollyea immediately, his phone number is 720-848-8084.

Who do I call if I have questions?

The researcher carrying out this study is Dr Daniel Pollyea. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr Daniel Pollyea at 720-848-8084. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr Pollyea with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

A description of this clinical trial will be available on http://www.Clinical Trials.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 will see my research information?

The University of Colorado Denver, Anschutz Medical Campus (CU Anschutz) and its affiliated health systems have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver, Anschutz Medical Campus
- University of Colorado Health

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Daniel Pollyea, MD
University of Colorado, Anschutz Cancer Pavilion
1665 Aurora Court, Mail Stop F754
Aurora, CO 80045 United States

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- The Institutional Review Board that is responsible for overseeing this research
- The study doctor and the rest of the study team.
- Members of your care team that have access to your electronic medical records.
- Karyopharm, who is providing funding support this research study.
- Officials at CU Anschutz, University of Colorado Health, Providers affiliated with your care, and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* of the following health information about you collected in this study available to:

- Karyopharm (drug manufacturer)
- UCD School of Pathology, Department of Pathology (Laboratory)
- Colorado Genetics Laboratory (CGL) (Laboratory)

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)

- Your social security number
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records (including study diary or questionnaire)
- Testing for or infection with diseases reportable to the Public Health department, including but not limited to: Human Immunodeficiency Virus (HIV), hepatitis (all forms) tuberculosis, or other sexually transmitted diseases.
- Tissue samples and the data with the samples.
- Billing or financial information

Your care team, including family doctor, may be made aware of your participation in the study through your electronic medical records.

What happens to Data, Tissue, Blood and Specimens that are collected in this study?

Scientists at the University and the health systems involved in this study work to find the causes and cures of disease. The data, tissue, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, tissue, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, the University or the health systems involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

The data we collect will be used for this study but may also be important for future research. Your data may be used for future research or distributed to other researchers for future study without additional consent if information that identifies you is removed from the data.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____ Date:_____

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name:_____

----------Use the following only if applicable----------

A signature of a witness is required for consent of non-reading subjects and consent using a short form

Witness of Signature ☐

Witness of consent process ☐

Interpreter/Witness Signature: _____ Date:_____

Print Name:_____