Institutional Review Board
Informed Consent Document for Research
MASTER CONSENT

Study Title: VCHEM23008P—A Phase Ib Study of Eltanexor (KPT-8602) and Venetoclax in Relapsed or Refractory Myelodysplastic Syndrome and Acute Myeloid Leukemia
Version Date: 04APR2024 NCT06399640

Part 1 of 2: MASTER CONSENT

Name of participant:_____ Age:_____

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

The purpose of this study is to learn if the investigational drug eltanexor (also known as KPT-8602) can help your condition when used in combination with the drug venetoclax (also known as Venclexta).

Investigational means that eltanexor is still being tested in research studies and has not yet been approved by regulatory health authorities, such as the U.S. Food and Drug Administration (FDA). Venetoclax is approved by the FDA for treatment of chronic lymphocytic leukemia (CLL) associated with a genetic change called 17p deletion, in patients who have received at least one prior therapy for CLL, and in untreated AML in elderly patients. The approved regimen for the untreated AML indication is venetoclax in combination with azacitidine, decitabine, or low dose cytarabine. The approved venetodax dosing for this indication is continuous (i.e., 28 days of a 28-day cycle). The combination of eltanexor and venetoclax, however, is investigational in this study.

Cancer is the uncontrolled growth of human cells. The growth of normal human cells is controlled in multiple ways. In cancer cells, one or more ways to control cell growth has not worked, or has been interfered with, leading to uncontrolled cell growth. One specific way cancer cells continue to grow, is by getting rid of certain proteins called "tumor suppressor proteins" that would normally cause cancer cells to die.

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Eltanexor functions by trapping "tumor suppressing proteins" within the cell, thus causing the cancer cells to die or stop growing.

Venetoclax functions by inhibiting or slowing down a protein in the body called bcl-2, which helps in normal process by which old cells in the body are cleared (called apoptosis). In diseases such as cancer, it is thought that failure to appropriately kill and clear old cells helps abnormal cancer cells to grow and multiply. By 'inhibiting an inhibitor' of apoptosis, venetoclax thus helps to increase the rate at which cancer cells get cleared from the body.

Eltanexor has previously been tested in humans to define its proper dose when used by itself. However, eltanexor has not been previously studied in combination with venetoclax for studies in humans. Thus, the main purpose of this study is to confirm the safe dose of eltanexor for use in combination with venetoclax.

It is not known at this time if eltanexor in combination with venetoclax will help your particular disease. This study will examine the effects, if any, of eltanexor and venetoclax on your disease and on your body, including any side-effects that you may experience. If you have a diagnosis of AML that did not respond to or progressed after prior treatment, you may be foregoing treatment option with known survival benefit in order to participate in this study.

This research study was developed at Vanderbilt University Medical Center (VUMC). Somedeb Ball, MD at the Vanderbilt-Ingram Cancer Center (VICC) is the sponsor-investigator (also known as the study chair) of this study.

This study is funded by the National Cancer Institute (National Institute of Health). Karyopharm Therapeutics Inc., the company who makes eltanexor have agreed to provide the medication at no cost for the purposes of this study. Karyopharm Therapeutics Inc. could benefit financially from this research study.

In this study, different doses and schedules of eltanexor will be tried with fixed dose and schedule of venetoclax to find out the most safe and effective dose and schedule of this combination treatment.

This study will be conducted at Vanderbilt University Medical Center with additional possibility of enrollment at one to two other centers. Overall, up to 60 patients are expected to join this study in about 2 years.

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Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have been diagnosed with Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML). Your condition either did not respond to prior treatment; or initially responded to, but then stopped responding to prior treatment.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

Side effects and risks that you can expect if you take part in this study:

Participation in any research study involves risk. During the study, you may have discomforts and risks from eltanexor, from venetoclax, and from the study procedures.

Most of these are listed here, but there may be others that we cannot predict. Discomforts and risks may vary from person to person.

Everyone taking part in the study will be monitored for discomforts and risks. However, doctors do not know all the discomforts and risks that may happen. They may be mild or very serious, and in some cases may be long-lasting or may never go away. Your study doctor may give you medications to help lessen some of the discomforts and risks.

Some risks described in this consent form as well as other unknown risks, if severe, may cause death.

You should talk to your study doctor about any discomforts and risks that you may have while taking part in this study. If a severe reaction to the study treatment occurs, your study doctor may interrupt or stop the study treatment.

You may experience some, none, or all of these potential discomforts and risks. They may be mild, moderate, or severe. **If any discomforts or risks occur, you must tell your study doctor.**

You must tell your study doctor about all medications (both prescribed and over-the-counter), vitamins and herbal remedies you are taking while participating in this study. Medications, vitamins and herbal remedies may affect the way the study treatment is metabolized by your body.

Risks of Eltanexor (also known as KPT-8602)

Commonly reported side effects of eltanexor (seen in greater than or equal to 10% of patients i.e., in 100 people receiving eltanexor more than 10 people may have):

- Nausea
- Loss of appetite
- Diarrhea
- Tiredness or fatigue
- Change in taste
- Vomiting
- Low counts of white blood cell and neutrophil (cells that protect you from infection): can make you prone to catch infection
- Low count of platelets (cells that help stop bleeding): can make you at risk of bleeding
- Low count of red blood cell: may cause weakness, tiredness, headache, or shortness of breath
- Temporary change in electrical activity of heart (we call Long QT interval on ECG)
- Weight loss
- Low sodium levels in your blood (side effects may include nausea, vomiting, headache, confusion and fatigue)
- Blurred vision
- Constipation
- Spread of infection in bloodstream (we call sepsis)

To help prevent some of these side effects, you may be prescribed medications to take prior to taking eltanexor.

Side Effects from Other Medications Used to Manage Decreased Appetite or Nausea
In addition to eltanexor, you may be prescribed other medications to help manage side effects such as decreased appetite or nausea. The medications listed below may relieve anorexia or nausea but also may result in side effects. Eltanexor can reduce your appetite so you may not be very hungry, especially in the first few weeks when you start therapy. It is very important to maintain your normal food and

fluid intake, and your weight during the study. Your study doctor can suggest ways to help you to maintain your normal intake of food and fluids and avoid losing weight. Please check your weight every day and inform your healthcare practitioner if you lose weight. Maintaining your normal food and fluid intake, and your weight, may reduce feelings of fatigue while you are taking eltanexor, and may reduce the risk of some of the other side effects. You and your doctor will discuss your treatment options and determine what choice may work best for you.

- Ondansetron: headache, diarrhea, fever, constipation, rash, flushing and temporary changes in heart rhythm.

Risks of Venetoclax (also known as Venclexta)

Patients with cancer have a risk of death due to their underlying disease or as a complication of their cancer treatment. The risk of side effects or death related to venetoclax will be closely monitored.

Treatment with venetoclax has been associated with nausea, diarrhea, decreases in lymphocytes and neutrophils (two different types of white blood cells), tumor lysis syndrome (TLS) and infections.

TLS is a problem that can occur when cancer cells break down rapidly and the body has to get rid of the broken up cell parts. Sometimes your body, especially the kidneys, can't remove the cell parts quickly enough, so the level of some of these cell products in your blood, such as salts and acids, can rise. This can happen especially in patients with large tumors or a high number of cancerous white cells in the blood.

Tumor lysis syndrome (TLS) can lead to serious problems such as effects on your kidney and heart (including abnormal heart rhythms) or seizures. These side effects can result in needing kidney dialysis (a special machine to remove toxins from the blood) and can lead to death. If you develop TLS, your study doctor will closely monitor and treat you as needed to try to reduce and prevent these complications. For your safety, your study doctor may decide to admit you to the hospital before or after you start venetoclax, in order to give fluids into your vein, do blood tests, and check for TLS. If you develop TLS, your urine may look dark, thick, or cloudy. You may experience fever, chills, nausea (feeling sick to your stomach), vomiting, diarrhea, confusion, shortness of breath, irregular heartbeat, unusual tiredness, muscle pain, joint discomfort and/or seizure. If you notice any of these, notify your study doctor or nurse right away.

Common side effects of venetoclax (may affect greater than 10% of patients):

- Upper respiratory tract infection –signs include runny nose, sore throat, or cough
- Low levels of red blood cells that carry oxygen throughout your body (anemia)
- Low counts of white blood cell and neutrophil (cells that protect you from infection): can make you prone to catch infection
- Low number of platelets (cells that help your blood clot): can increase risk of bleeding
- Higher level of phosphorous in blood test (hyperphosphatemia) (side effects may include musde and/or joint paint, muscle weakness, itching and red eyes, constipation, nausea, vomiting and diarrhea)
- Decreased levels of potassium in your blood (side effects may include muscle weakness, muscle pain, tremors, muscle cramps, and constipation)
- Diarrhea
- Feeling or being sick (nausea or vomiting).
- Constipation
- Feeling tired
- Fever
- Headache

Other side effects of venetoclax (may affect from 1% up to 10% of patients):

- Respiratory tract infections. including Pneumonia (infections of the sinuses, throat airways and/or lungs)
- Conjunctivitis (inflammation of the eyes)
- Infections (viral, bacterial and fungal)
- Herpes Zoster (shingles) (side effects include painful rash)
- Urinary tract infection
- Fever with low number of white blood cells (febrile neutropenia)
- Peripheral edema (swelling of the hand and/or feet)
- Tumor lysis syndrome –described above; may experience fever, chills, nausea (feeling sick to your stomach), vomiting, diarrhea, confusion, shortness of breath, irregular heart beat, unusual tiredness, muscle pain, joint discomfort and/or seizure
- Higher level of uric acid (hyperuricemia) (side effects include pain, inflammation, swelling and tenderness in the joints)
- Lower level of calcium (hypocalcemia) (side effects include confusion or memory loss, muscle spasms, numbness/tingling in the hands feet and face, depression, hallucinations, muscle cramps, weak and brittle nails, easy fracturing of bones)

- Higher level of potassium (hyperkalemia) (side effects include tiredness, numbness/tingling, nausea, vomiting, difficulty breathing, chest pain, palpitations or irregular heartbeat)
- Higher level of creatinine (blood creatinine increase) which may indicate injury or damage to the kidneys

Reproductive Risks

Female patients:

Patients should not become pregnant while on this study because the study treatments can affect an unborn baby. Breast-feeding and pregnant women are not allowed to take part in the study. Due to unknown risks and potential harm to an unborn child/infant, you should not become pregnant or nurse a baby while on this study or for 3 months following the last dose of study tre atment. Females able to have a child must have a negative pregnancy test prior to enrolling in the study. Female patients must meet 1 of the following conditions:

- Patient is postmenopausal –i.e., amenorrheic (no menstrual period) without an alternative medical cause – for at least 1 year prior to the date of signed informed consent (note: postmenopausal status in females < 62 years of age should be confirmed with a serum FSH level within laboratory reference range for postmenopausal women), or
- Patient is surgically sterile (i.e., patient has had a bilateral tubal ligation, a bilateral oophorectomy, or a complete hysterectomy), or patient's partner is surgically sterile (i.e., has had a vasectomy), or
- If of childbearing potential, female patient agrees to practice 2 methods of contraception (one highly effective and one effective) at the same time, from the time of signing the informed consent through 3 months after patient's last dose of eltanexor or venetoclax (whichever dose occurs last), or
- Patient agrees to practice true abstinence (defined as complete avoidance of heterosexual intercourse), when this is in line with the preferred and usual lifestyle of the patient.

Male patients:

You should not father a child while on this study or for 3 months after your last dose of study treatment because the treatments in this study can affect an unborn baby. Participation in this study may affect your ability to father a child. For future childbearing, you should consider banking sperm prior to beginning this study. Due to unknown risks and potential harm to an unborn child/infant, you should not get a partner pregnant while you are getting the study treatment. Male patients must meet 1 of the following conditions:

- Patient is surgically sterile (has had a vasectomy), or patient's sexual partner is post-menopausal or surgically sterile (i.e. patient has had a bilateral tubal ligation, a bilateral oophorectomy, or a complete hysterectomy), or
- Patient agrees to practice effective barrier contraception from the time of signing the informed consent through 3 months after patient's last dose of eltanexor or venetoclax (whichever dose occurs last), or
- Patient agrees to practice true abstinence (defined as complete avoidance of heterosexual intercourse), when this is in line with the preferred and usual lifestyle of the patient.

All patients (male or female):

- If your partner becomes pregnant during this study, you must tell the study doctor immediately. The study doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you. For female patients who become pregnant while on this study, the study treatment will be stopped immediately and the pregnancy will be followed until conclusion. For partners of male patients who become pregnant, the partners will be asked to consent for their pregnancy will be followed until conclusion.

Highly effective methods of contraception (birth control) include:

- Hormonal contraceptives (for example, combined oral contraceptives, patch, vaginal ring, injectables, and implants).
- Intrauterine device or intrauterine system.
- Vasectomy or tubal ligation.

Effective methods of contraception (birth control) include:

- Barrier methods of contraception (for example, male condom, female condom, cervical cap, diaphragm, contraceptive sponge).

Contraception 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 women who have given birth (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 (for example, 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.
- Total (true) abstinence (when this is in line with the preferred and usual lifestyle of the patient), is an acceptable method of contraception. However, periodic abstinence (for example, calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.

Additional Risks

Allergic Reaction

It is possible to have an allergic reaction to the study treatment. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are- rash, having a hard time breathing, wheezing, a sudden drop in blood pressure (making you feel dizzy or lightheaded), swelling around the mouth, throat, or eyes, a fast pulse or sweating.

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

Electrocardiogram (ECG)

An ECG is a test that measures the electrical activity of your heart. It involves putting sticky pads on your skin while the electrical activity of the heart is recorded. Skin irritation, redness, itching, or pain when removing the ECG leads is a possible risk. If the skin under the patches needs to be shaved, irritation from shaving also could occur.

Blood Draw Risks

When you give blood, you may feel faint, or experience mild pain, bruising, irritation or redness at the site. In rare cases, you may get an infection.

Bone Marrow Aspiration and Biopsy

A biopsy or aspirate is a procedure used to remove a piece of tissue or a sample of cells from your body so that it can be analyzed in a laboratory. For most cancers, the only way to make a definitive diagnosis is to perform a biopsy to collect sample of cells in order to characterize of your specific cancer. The type of biopsy procedure used will depend upon the location and kind of tissue that will be sampled. You may have side effects from this procedure, which may include fainting, bleeding, bruising, discomfort, dizziness, infection and/or pain at the puncture or incision site, and at the site from which the tissue is removed.

Your doctor will describe the procedure to be used for your cancer in detail and will answer any questions and address any concerns you may have. Bone marrow biopsies or aspirates are required for this study unless your doctor feels that the procedure could seriously harm you.

Privacy Risks

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

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 comes from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only Dr. Ball and his team will have access to your name.

Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Good effects that might result from this study:

a. The benefits to science and humankind that might result from this study:
This research may contribute to a better understanding of cancer and its treatment, and may eventually lead to improvements in treatment.

b. The benefits you might get from being in this study:
There may or may not be a direct benefit to you as a result of your participation in this study.

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Other treatments you could get if you decide not to be in this study:
There may be other treatment options that are available to you, including receiving standard therapies. You should speak to your doctor about all of your treatment options prior to deciding to participate in this study.

Payments for your time spent taking part in this study or expenses:
You will not be paid for participating in this study.

Procedures to be followed:

If you qualify and agree to participate, your time in this research study will be followed in "Cycles". Each treatment Cycle lasts 28 days.

All patients participating in this study will receive treatment with eltanexor and venetoclax.

Eltanexor and venetoclax are both oral medications that you will take by mouth:

- Eltanexor: Five days per week for 4 weeks (dose levels 1 and 3), 3 weeks (dose levels 2 and -1) or 2 weeks (dose level -2)
- Venetoclax: Dosed once daily on Days 1 to 14

It is intended that you will take eltanexor and venetoclax until your disease gets worse, until you have unacceptable side effects, or for up to 12 months. After 1 year of treatment, if your disease is responding to treatment and your study doctor, the sponsor-investigator at Vanderbilt, and the drug suppliers agree, you may be allowed to continue on study treatment.

Venetoclax should be taken with food and water at the same time each day, generally within 30 minutes of a meal. The tablets should be swallowed whole and not crushed or broken. You should drink 6-8 glasses of water daily for two days before initiating therapy with venetoclax.

Eltanexor should be dosed with, or within 30 minutes of solid food consumption, together with at least 120ml of water. Tablets should be swallowed whole and not crushed or chewed.

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You will be given a diary to complete while you are taking the study medications. This is to record the date, time, and how much of each study drug you have taken. You will be asked to return your completed diary when you come to the clinic for each visit.

If you decide to participate in the study, you must first sign this consent form. Before you are treated, your study doctor will need to determine if you are eligible to take part in this study. By signing this form, you agree to follow the instructions given by the research staff during the study.

After reviewing and signing this consent form, you will be asked to undergo tests and procedures to find out if it is okay for you to take part in the research study. This is called screening. Some of these tests and procedures are likely to be part of the regular care you would receive even if you were not participating in the study. You may have had some of these tests or procedures recently. If this is the case, these tests or procedures may not need to be repeated.

After these tests are reviewed, it is possible you will not be able to join the study. There may be other reasons why you are unable to be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Brief summary of all activities on study are listed in the table below.

Table. Study Calendar- List of Scheduled Activities in the Study

Procedures	Screening Visit Day -14 to -1	Cycle 1 Day 1	Cycle 1 Day 2-3	Cycle 1 Days 8,15, 22	Cycle 2 Day 1 +/- 3 days	Cycle 2 Day 15 +/- 3 days	Cycle 3 Onwards: Day 1 +/- 3 days	End of Treatment Visit (≤10d after last study dose)	Follow-Up (28d +/- 7d after last study dose)
Informed Consent	X								
Physical Examination	X	X		X	X	X	X	X	X
Performance Status	X	X			X		X	X	X
Height	X								

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Procedures	Screening Visit Day -14 to -1	Cycle 1 Day 1	Cycle 1 Day 2-3	Cycle 1 Days 8,15, 22	Cycle 2 Day 1 +/- 3 days	Cycle 2 Day 15 +/- 3 days	Cycle 3 Onwards: Day 1 +/- 3 days	End of Treatment Visit (≤10d after last study dose)	Follow-Up (28d +/- 7d after last study dose)
Weight	X	X		X	X	X	X	X	X
Vital Signs	X	X	X	X	X	X	X	X	X
Blood Tests	X	X	X	X	X	X	X	X	X
Urine Test	X							X	
Pregnancy Test	X	X						X	
ECG	X							X	
Bone Marrow Biopsy	X			Day 8	X		Cycle 5 Day 1	Only for Disease Progression	
Receive Study Medications		X			X		X		
Monitoring for Side Effects	X———————————————————————————————————X								

Screening

The following must be completed ≤ 14 days prior to your first dose of study treatment:

- History taking and physical exam. You will be asked about your past and current health including any past treatments for your condition. A general physical examination will be conducted by study doctor at a clinic visit.
- Nutritional counseling. You may experience certain gastrointestinal side effects while being in this study and ways to reduce or prevent some of these side effects will be discussed.
- Your performance status will be assessed by questions about your ability to carry out daily activities, and your height and weight will be recorded.
- Height and weight measurements.

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- Vital Signs: Blood pressure (BP), heart rate (HR) and temperature.
- You will be asked about any problems you are having and recent or current medicines you are taking (including all prescriptions, over-the-counter medicines, vitamins, dietary supplements, and herbal preparations).
- Blood will be drawn (about 1 tablespoon) to check the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
  - Check proteins associated with muscle inflammation, digestion, thyroid function, and your blood's ability to clot
  - Women Only: A blood pregnancy test will be done for women who can have children (about ⅓ tablespoon of blood will be drawn) within 3 days of starting the study treatment. The pregnancy test must be negative for you to take part in the study. Women who are pregnant or breast feeding may not take part in the study. If you are a post-menopausal woman (a woman who can no longer become pregnant) < 62 years of age, a portion of the above blood collected for blood chemistries may be used to also measure follicle stimulating hormone (FSH) to confirm your post-menopausal status.
- Additional blood may be drawn (about 1 - 2 tablespoons) for pharmacodynamic (PD) blood samples to study how your body and illness may be reacting to the study medications that you are receiving.
- Urine test (about ¼ cup of urine will be collected) to check your kidney function and assess for

other abnormalities of your urinary tract.

- 12-Lead electrocardiogram (ECG) to check the electrical activity of your heart, using 12 sticky pads attached to the surface of your skin.
- Bone marrow aspiration and biopsy: At least 10-15 mL (about 2 - 3 teaspoons) of bone marrow aspirate material must be available from a fresh or recent bone marrow biopsy procedure done ≤ 14 days prior to starting study treatment.

Treatment

If, based on the results of the above screening tests and procedures, you qualify and choose to participate in the study, you will return to your study doctor's office to begin treatment.

As discussed further below in this consent document, one of the risks of the study treatment is Tumor Lysis Syndrome (TLS).

TLS is a problem that can occur when cancer cells rapidly break down, and the body must get rid of broken-up

cell parts. Sometimes your body cannot remove the cell parts quickly enough, so the level of some products in your blood, such as salts and acids, can rise. This can happen especially in patients with a high number of white cells in the blood.

TLS can lead to serious problems such as effects on your kidney and heart (including abnormal heart rhythms) or seizures. These side effects can result in needing kidney dialysis (a special machine to remove toxins from the blood) or lead to death.

If you develop TLS, your urine may look dark, thick, or cloudy. You may experience fever, chills, nausea (feeling sick to your stomach), vomiting, diarrhea, confusion, shortness of breath, irregular heartbeat, unusual tiredness, muscle pain, joint discomfort and/or seizure. If you notice this, notify your study doctor or clinic staff right away.

To help prevent TLS and closely monitor you for signs of TLS:

- Your study doctor will closely monitor and treat you as needed to decrease the risk of any serious changes in your blood or other complications of TLS. If blood tests suggest the occurrence of TLS, extra blood tests or monitoring of your heart rhythm may be recommended by your study doctor. Depending on your condition, your study doctor may also admit you to the hospital prior to, during, or after you start the study treatment, in order to help prevent or treat TLS.
- Before starting study treatment and continuing throughout the study, your study doctor will ask you to drink plenty of fluids.

Prior to receiving your first dose of venetoclax, you will receive treatment to reduce the risk of TLS. At

least 2-3 days before you start study treatment, your study doctor will give you medication (such as allopurinol) to help your body get rid of broken up cell parts from your cancer. Allopurinol, usually given as an oral drug, helps prevents buildup of uric acid in the blood and is commonly used in other settings to treat gout and kidney stones.

Dosing Diary:

- You will be given a dosing diary to complete while you are taking the study medications. This is to

record the date, time, and how much study medication you have taken. You will be asked to return your completed diary when you come to the clinic for each visit.

- You will be asked to confirm if you took your dose with food.
- You may also record any problems you have had while taking the study medication or any questions you may have for the study doctor or nurse. You will be asked to bring any unused study drug along with any empty bottles with you to each clinic visit.

Cycle 1, Day 1

- Weight
- Vital Signs: BP, HR, and temperature assessments
- You will be asked about any problems you are having and the medicines you are taking
- Preventative treatment (prophylaxis) against TLS:
  - Continue drinking plenty of fluids
  - Continue allopurinol
  - Receive intravenous (IV) fluids as needed, typically into a vein in your arm. You will need to travel to your study doctor, in order to receive IV fluids, typically into a vein in your arm
- Start eltanexor and venetoclax
- Before beginning eltanexor, you will receive medicine called an "antiemetic", to help prevent nausea and vomiting. This medicine is usually an oral drug given by mouth, such as ondansetron. On Cycle

1, Day 1, you will take ondansetron or similar medicine against nausea and vomiting at least 1 hour before starting eltanexor

Unless previously completed ≤ 3 days prior to your first dose of study treatment:

- Physical exam
- Your performance status (ability to carry out your daily activities) will be assessed
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
  - Women Only: A blood pregnancy test will be done for women who can have children (about ⅓ tablespoon of blood will be drawn).

Cycle 1, Days 2 and 3

- Physical exam
- Vital Signs: Blood pressure (BP), heart rate (HR) and temperature
- You will be asked about any problems you are having and the medicines you are taking
- Continue eltanexor and venetoclax
- Continue antiemetics
- Preventative treatment (prophylaxis) against TLS:
  - Continue drinking plenty of fluids
  - Continue allopurinol. Note you will continue allopurinol at least during your first 28 days of study treatment (i.e. until completion of Cycle 1).
  - Receive intravenous (IV) fluids as needed. You will need to travel to your study doctor, in order to receive IV fluids, typically into a vein in your arm. It is also possible that your study doctor will admit you to the hospital for fluids, monitoring, and additional treatment against Tumor Lysis Syndrome.
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)

Cycle 1, Day 8

- Physical exam
- Weight
- Vital Signs
- You will be asked about any problems you are having and the medicines you are taking
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
- You are scheduled to receive your first weekly doses of eltanexor. But before the eltanexor dose, you will receive antiemetic again to help prevent nausea and vomiting.
- An additional bone marrow aspiration and biopsy will be performed
- An additional (PD) blood sample (about 1-2 tablespoons) will be collected to study how your body and illness may be reacting to the study medications that you are receiving

Cycle 1, Days 15 and 22

- Physical exam
- Weight
- Vital Signs
- You will be asked about any problems you are having and the medicines you are taking
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
- On Cycle 1, Days 15 and 22: you are scheduled to receive your first weekly doses of eltanexor. But before the eltanexor dose, you will receive antiemetic again to help prevent nausea and vomiting.

Cycle 2, Day1 and Cycle 5, Day 1

- Physical exam
- Your performance status (ability to carry out your daily activities) will be assessed
- Weight and height
- Vital signs
- You will be asked about any problems you are having and the medicines you are taking
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
- On these days, fresh bone marrow biopsy and aspirate will be collected
- PD blood sample (about 1-2 tablespoons) will be collected prior to scheduled bone marrow procedure

Cycle 2, Days 15

- Physical exam
- Weight
- Vital Signs
- You will be asked about any problems you are having and the medicines you are taking
- Blood will be drawn (about ½ tablespoon) for the following:

  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
- Before the eltanexor dose, you will receive antiemetic again to help prevent nausea and vomiting.

Cycles 3, 4, and 6+ Day 1

In general, you may continue to receive study treatment for up to 12 months as long as you tolerate treatment, and your disease does not get worse (progress). After 1 year of study treatment, you may be allowed to continue treatment, if your study doctor at Vanderbilt and Karyopharm Therapeutics, Inc. agree that your disease is still responding to the treatment, and you continue to receive benefit.

If you continue beyond Cycle 1, the following will occur on Day 1 of each new 28-day cycle (excluding Cycle 2 and Cycle 5 which are described above):

- Physical exam
- Your performance status (ability to carry out your daily activities) will be assessed
- Weight and height
- Vital signs
- You will be asked about any problems you are having and the medicines you are taking
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)

End-of-Treatment and Follow-up

You may stop receiving study treatment based on your disease assessments, or if you are having side effects that make you unable to tolerate study therapy. Based on discussions between you and your study doctor, you may discontinue for other reasons including your decision to stop being treated.

End-of-Treatment / Withdrawal Assessments

The following must be completed subsequent to and not later than 10 days after your last dose of study treatment with eltanexor or venetoclax (whichever treatment occurs last) and prior to any subsequent anti-cancer therapy:

- Physical Exam
- Your performance status (ability to carry out your daily activities) will be assessed

- Weight
- Vital signs: BP, HR, and temperature
- You will be asked about any problems you are having and the medicines you are taking
- Blood will be drawn (about 1 tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)
  - Check proteins associated with muscle inflammation, digestion, thyroid function, and your blood's ability to clot
  - Women Only: A blood pregnancy test will be done for women who can have children (about ⅓ tablespoon of additional blood will be drawn)
- Urine test (about ¼ cup of urine will be collected) to check your kidney function and assess for other abnormalities of your urinary tract
- 12-Lead ECG to check the electrical activity of your heart, using 12 sticky pads attached to the surface of your skin
- Pharmacodynamic blood samples (about 1 - 2 tablespoons of blood) to study how your body and illness may be reacting to the drugs that you are receiving
- A fresh bone marrow biopsy is required only in the event of suspected relapse or progression

Also, if your disease is monitored by bone marrow procedure and you discontinue study treatment for reason other than progressive disease confirmed by marrow procedure (for example, because of blood tests suggesting your illness may be getting worse), please note the study may continue to request results of laboratory tests that you have done outside of the study (but which are related to peripheral blood counts or bone marrow examination), until progression of your disease following eltanexor/venetoclax treatment is ultimately confirmed by bone marrow procedure.

28-Day Follow-Up Visit Assessments

You will be asked to return to the study clinic 28 (+7) days after your final treatment with eltanexor or venetoclax (whichever occurs last), in order to undergo the following:

- Physical Exam
- Your performance status
- Weight
- You will be asked about any problems you are having and the medicines you are

taking
- Vital signs
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your blood cell counts (numbers of each type of blood cell)
  - Check your blood chemistries (proteins, elements and minerals in your blood)

Long-Term Follow-Up

After you complete all of the planned study visits, you will be contacted approximately every 3 months (± 14 days) after your final treatment with eltanexor or venetoclax (whichever occurs last), in order to determine your health status. Contact could be by a variety of methods, including via telephone, clinic visit, medical records, or publicly available information. This will continue until death, end of the study, until you withdraw consent for this communication, or for a maximum of 2 years after your final treatment with eltanexor/venetoclax – whichever comes first.

Reasons why the study doctor may take you out of this study:

The study doctor, sponsor, or a regulatory authority (FDA, Institutional Review Board, etc) may choose to end your participation in this study without your consent. This could happen for reasons such as:

- The study doctor feels it is not in your best interest to continue in the study,
- You fail to follow the study doctor's instructions,
- You experience an adverse reaction that requires other medical treatment,
- You become pregnant, or
- The sponsor, drug providers, or the FDA or other regulatory authority stops the study for any reason.

If you are removed from the study, the reason will be explained to you. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Study Title: VCHEM23008P– A Phase Ib Study of Eltanexor (KPT-8602) and Venetoclax in Relapsed or Refractory Myelodysplastic Syndrome and Acute Myeloid Leukemia
Version Date: 04APR2024

Clinical Trials Registry:
A description of this clinical trial will be available on 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.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you.

This research will include standard somatic specimen sequencing, but will not include whole genome or human germline sequencing.

Study Results:
After the study is finished, the research data that has been put into your medical record will be kept for at least six years. The research data that has not been put in your medical record will be kept for an unknown period of time. You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

Institutional Review Board
Informed Consent Document for Research
STUDY SITE INFORMATION

Study Title: VCHEM23008P | A Phase Ib Study of Eltanexor (KPT-8602) and Venetoclax in Relapsed or Refractory Myelodysplastic Syndrome and Acute Myeloid Leukemia

Version Date: 09APR2024

Part 2 of 2: STUDY SITE INFORMATION

Site Name:	Vanderbilt University Medical Center
Site Principal Investigator:	Somedeb Ball, MD
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

This part of the consent form includes information about the site that is asking you to participate in this study and is specific to participation at your site only. Before making your decision, both the site-specific information and the general study information should be reviewed with you. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research; however, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt to treat the injury.

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There are no plans for Vanderbilt, Karyopharm, or Abbvie to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt, Karyopharm, or Abbie to give you money for the injury.

Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please contact [redacted]

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Medical Center Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Additional information about your local site:

This research study was developed at Vanderbilt University Medical Center (VUMC). Somedeb Ball, MD at the Vanderbilt-Ingram Cancer Center (VICC) is the sponsor-investigator (also known as the study chair) of this study. This study is funded by the National Cancer Institute (National Institute of Health). Karyopharm Therapeutics Inc., the company who makes eltanexor have agreed to provide the medication at no cost for the purposes of this study. Karyopharm Therapeutics Inc. could benefit financially from this research study.

Confidentiality:

All efforts, within reason, will be made to keep your personal information in your research record confidential but total confidentiality cannot be guaranteed. Your information and samples will be given a unique code instead of your name to help protect your identity. Dr. Ball, his staff at Vanderbilt and other authorized people will be the only people who know your personal information. Results of this study may be presented in meetings or in publications. Your identity will not be released in those presentations. Your study records will be secured in the clinical trials office. Your research data will be kept for an unknown period of time. Your tissue and blood samples will be kept in locked storage and may be used or stored indefinitely from the end of the study. Any samples that are not needed will be destroyed.

Vanderbilt may share your information, without identifiers, to others including the drug providers or use it for other research projects not listed in this form. Vanderbilt, Dr. Ball, and his

staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Ball and his study team may share the results of your study and/or non-study linked blood and other tissue samples and related records, physical examinations, laboratory tests, imaging studies, ECG results, as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University

Institutional Review Board, domestic and foreign drug regulatory agencies such as the Food and Drug Administration, National Institutes of Health, National Cancer Institute, representatives of Karyopharm

Therapeutics, clinical research organizations, Scientific Review Committees, Medicare and Insurance companies for billing purposes, etc. Federal privacy rules may not apply to these

groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.
The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Ball in writing and let him know that you withdraw your consent. His mailing address is: [redacted]. At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

Future Contact
We may want to contact you in the future to see if you would be interested in taking part in future studies. This will not affect the status of this study.

Please check Yes or No to the questions below:
___ Yes, you can contact me about future studies.
___ No, I may not be contacted about future studies.

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Version Date: 09APR2024

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
	Printed Name and Title

Time: _____