THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase I Study of Liposomal Cytarabine and Daunorubicin (CPX-351) in Combination with Gemtuzumab Ozogamicin (GO) in Relapsed Refractory Pediatric Patients with Acute Myeloid Leukemia (AML)

2020-0484

Study Chair: Branko Cuglievan

_____ _____
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

If you are reading and signing this form on behalf of a potential participant, please note: Any time the words "you," "your," "I," or "me" appear, it is meant to apply to the potential participant.

The goal of this clinical research study is to find the recommended dose of CPX-351 (a combination of cytarabine and daunorubicin) that can be given in combination with gemtuzumab ozogamicin (GO) to pediatric patients with relapsed (has returned after treatment) or refractory (has not responded to treatment) acute myeloid leukemia (AML). The safety and effects of the drug combination will also be studied.

This is an investigational study. CPX-351 and GO are both FDA approved and commercially available for the treatment of AML. It is considered investigational to give CPX-351 in combination with GO to pediatric patients with relapsed/refractory AML. The study doctor can explain how the study drugs are designed to work.

The study drug(s) 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. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

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

You will receive CPX-351 and GO for up to 3 cycles. Your total participation on this study (including screening and follow-up) should last up to 5 months.

You and/or your insurance provider will be responsible for the cost of CPX-351 and GO.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard chemotherapy, radiation therapy, hormone therapy, a combination of radiation and immunotherapy, or other approved drugs. You may receive other investigational therapy, if available. The study doctor will discuss the possible risks and benefits of these treatments. 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 and procedures will be performed to help the doctor decide if you are eligible. Some of these tests will need to be performed within 21 days of your first dose of study drugs and some will need to be performed within 14 days.

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests and cytogenetic testing. Cytogenetic testing looks at how genetic changes to cells may affect how the disease may react to the study drug. This sample will also be used to check the status of the disease and to check for viruses (hepatitis B and C and HIV [the AIDS virus]). Throughout this study, your blood draws for routine testing may be performed at a lab closer to your home.
- You will have an EKG and an echocardiogram (ECHO) or MUGA scan to check your heart function.
- You will have a bone marrow biopsy/aspirate to check the status of the disease. To collect a bone marrow biopsy/aspirate, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow and/or bone is withdrawn through a large needle.
- If you can become pregnant, part of the above blood sample or a urine sample will be collected 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 this study, you will not be enrolled. Other options will be discussed with you.

Up to 18 participants will be enrolled in this study. All will take part at MD Anderson.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a dose level of CPX-351 and GO. All participants will receive the same starting dose of CPX-351 and GO. If intolerable side effects are seen in the starting dose, the next group of participants will receive a lower dose level. If intolerable side effects are seen in the lower dose, the next group of participants will receive the lowest dose level.

Study Drug Administration

Each phase is 28 days.

This study has up to 3 phases: **1st Induction**, **2nd Induction**, and **Consolidation**.

During the **1st Induction** phase, you will receive CPX-351 by vein over about 90 minutes on Days 1, 3, and 5. You will also receive GO by vein over about 2 hours on Day 1 only.

If the disease does not respond to the study drugs by the end of the 1st Induction phase, you will begin the **2nd Induction** phase. During 2nd Induction, you will receive CPX-351 by vein over about 90 minutes on Days 1 and 3. You will also receive GO by vein over about 2 hours on Day 1 only.

If the disease does respond to the study drugs in the 1st Induction phase, you will not take part in the 2nd Induction phase.

About 4 weeks after your last induction, you will begin the **Consolidation** phase. During Consolidation, you will receive CPX-351 by vein over about 90 minutes on Days 1 and 3. You will also receive GO by vein over about 2 hours on Day 1 only.

If the doctor thinks it is in your best interest, you may be admitted to the hospital to receive the study drugs.

During this study, you will also be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information on how the drugs are given and their risks.

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.

Your participation on this study will be over after the End-of-Treatment Visit.

Study Visits

On **Day 1 of the First Induction Phase**:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests.

On **Day 1 of each following phase (2nd Induction and/or Consolidation):**

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine and cytogenetic testing and to check the status of the disease.
- If the doctor thinks it is needed, you may have an EKG and/or an ECHO or MUGA scan to check your heart function.
- You will have a bone marrow biopsy/aspirate to check the status of the disease before and after the Consolidation phase.

End-of-Study Visit

About 28 days after your last dose of study drugs, you will have an End-of-Study Visit. The following tests and procedures will be performed at this visit:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests, cytogenetic testing, and to check the status of the disease.
- You will have a bone marrow biopsy/aspirate to check the status of the disease. This sample may also be used for genetic testing.

If you are unable to come to the clinic for the End-of-Study Visit, the study staff will call you to check on how you are doing and any side effects you may have. This phone call should take about 5 minutes.

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 the study drug 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 the study drug. 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.

CPX-351 Side Effects

Common (occurring in more than 20% of patients)

• swelling • irregular heartbeat • heart damage • low blood pressure (possible dizziness/fainting) • headache • fatigue • difficulty sleeping • chills	• skin rash • diarrhea • nausea • inflammation of the intestines • mouth blisters/sores (possible difficulty swallowing) • constipation • abdominal pain	• loss of appetite • vomiting • bacteria in the blood • muscle and/or bone pain • cough • difficulty breathing

CPX-351 may cause low blood cell counts (red blood cells, platelets, and/or 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 platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia, severe fungal infection, 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)

• high blood pressure • chest pain • fever • dizziness • delirium (loss of contact with reality) • anxiety • hallucinations (seeing or hearing things that are not there) • itching • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• hemorrhoids • upset stomach • abnormal liver test (possible liver damage and/or yellowing of the skin and/or eyes) • eye dryness, pain, irritation, inflammation, redness, and/or swelling • vision problems • deafness • decreased kidney function • low oxygen level in the blood (possible lightheadedness)	• build-up of fluid around the lungs • lung inflammation (possible difficulty breathing) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • injection site swelling, pain, and/or heat

At this time, there are no known side effects that **occur in fewer than 3% of patients**.

You may continue to have low white blood cell counts after you stop taking CPX-351, putting you at risk for infection even after you stop taking the drug.

Gemtuzumab Ozogamicin (GO) Side Effects

Common (occurring in more than 20% of patients)

• heart damage • fatigue • fever • constipation • mouth blisters/sores (possible difficulty swallowing)	• nausea/vomiting • bleeding • abnormal liver test (possible liver damage and/or yellowing of the skin and/or eyes)	• liver damage (possibly due to blood clots) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

GO may cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Occasional (occurring in 3-20% of patients)

• headache • skin rash	• high blood sugar (possible diabetes)	• kidney damage • pain

GO may cause low white blood cell counts:

- 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.

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

• fast heartbeat • diarrhea	• bladder inflammation (possible pain and/or urge to urinate)	• lung inflammation (possible difficulty breathing) • fluid in the lung (possible difficulty breathing)

GO may also cause severe infusion-related reactions (possible chills and/or hives). It is not known how often this side effect may occur.

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.

Bone marrow biopsies/aspirates 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 and 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.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study. Only authorized study staff will have access to study data.

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. You must use birth control during the study and for 30 days after your last dose of study drugs if you are sexually active.

Birth Control Specifications: If you can become pregnant or father a child, you must use birth control during the study and for 30 days after you stop receiving the study drugs. Effective birth control methods include:

- Birth control pills, patches, shots, or implants
- Intrauterine devices (IUDs)
- Condom or occlusive cap (diaphragm or cervical/vault cap) with spermicide

Talk with the study doctor about what kind of birth control methods to use and how long to use them. Some methods may not be approved for use during this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. During this study and for 30 days after your last dose of study drugs, you should not donate sperm. You will need to use a condom while on this study and for 30 days after your last dose of study drugs.

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 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 will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Branko Cuglievan, at 713-729-2860) 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.

   If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can continue to collect data from your routine medical care. If you agree, this data will be handled the same as research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, 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 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.

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/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as 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.

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 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.

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

Genetic Research
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).

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
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   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.

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
(Adult Participants Only)

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 **2020-0484**.

_____ _____
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

PARENT/GUARDIAN PERMISSION

I have read and understand the description of this research. I have had a chance to discuss the study and ask questions. My questions have been answered. I give permission for my child or ward to take part in this study.

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE

_____
PRINTED NAME OF PARENT/GUARDIAN

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE
Signature of Other Parent (Optional, unless required by the IRB.)

_____
PRINTED NAME OF PARENT/GUARDIAN

____The IRB has determined that the signature of both parents is required.

If not obtaining both parental signatures, please indicate reason below:

____Other parent is deceased, unknown, incompetent, or not reasonably available.

____Parent/Guardian signing above has sole legal responsibility for the care and custody of the child.

__**X**__ The IRB has determined that the signature of both parents is NOT required.

WITNESS TO PARENTAL/GUARDIAN PERMISSION

I was present during the explanation of the research to be performed under Protocol **2020-0484**. The child participant was also present. In my opinion, the parent(s)/guardian provided permission for the child to participate in the research.

_____ _____
SIGNATURE OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____
PRINTED NAME OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION

ASSENT OF MINOR

(Entire section must be completed if the participant's intellectual age is at least 7 and less than 18 years. Participants with an intellectual age of 7 - 12 are not required to sign.)

If written assent is not obtained on an age-appropriate participant, check reason why not:

____ 1.) The participant's intellectual age is less than seven.

____ 2.) The participant dissented, but the participant's parent(s)/guardian felt that the intervention(s) or procedure(s) involved in the research hold out the possibility of a direct benefit that is important to the health and/or well being of the participant and is available only in the context of this research study.

____ 3.) Other: _____

I have been told what I will be asked to do in this study.

I have been told that I do not have to be in this study. If I decide not to be in this study, no one will be mad at me. I may quit at any time, but if I do, I may need to take a different treatment.

I have had a chance to talk about the study and ask the study doctor questions. All of my questions have been answered. I agree to be in this study and do what I am asked to do so long as I want to stay in this study. I agree that the study doctor can put me on this study. By signing this paper, I am not giving up any of my legal rights. I have been given a copy of this document.

_____ _____

SIGNATURE OF MINOR (Age 13-17) DATE

_____

PRINTED NAME OF MINOR

WITNESS TO ASSENT

I was present during the explanation of the research to be performed under Protocol **2020-0484**. The child participant was also present. In my opinion, the child assented to participate in the research. (Note: If obtaining assent, a witness signature is required.)

_____ _____

SIGNATURE OF WITNESS TO THE ASSENT (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____

PRINTED NAME OF WITNESS TO THE ASSENT

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