ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

PROTOCOL UPDATE TO ALLIANCE A041701

A RANDOMIZED PHASE II/III STUDY OF CONVENTIONAL CHEMOTHERAPY +/- UPROLESELAN (GMI-1271) IN OLDER ADULTS WITH ACUTE MYELOID LEUKEMIA RECEIVING INTENSIVE INDUCTION CHEMOTHERAPY

NCI-supplied agent: Uproleselan (GMI-1271) (NSC #801708, IND #[redacted] IND holder: DCTD
Commercial agent(s): Daunorubicin (NSC #82151), Cytarabine (NSC #63878)

[X]	**Update:**	[ ]	**Status Change:**
[ ]	Eligibility changes	[ ]	Activation
[ ]	Therapy / Dose Modifications / Study Calendar changes	[X]	Closure
[ ]	Informed Consent changes	[ ]	Suspension / temporary closure
[X]	Scientific / Statistical Considerations changes	[ ]	Reactivation
[X]	Data Submission / Forms changes		
[X]	Editorial / Administrative changes		
[X]	Other: Updated CTSU Boilerplate Language		

***If your site utilizes the CIRB as your IRB of record:* No recommended IRB level of review is provided by the Alliance since the CIRB is the IRB of record for this trial. The site has 30 days after the posting of this amendment to implement it at their site. Please refer to the amendment application and CIRB guidelines for further instructions.**

***If your site utilizes a local IRB as your IRB of record:* IRB approval (or disapproval) is required within 90 days. Please follow your local IRB guidelines. Expedited IRB Approval is allowed. The proposed changes in this amendment are minor and do not affect the overall risk/benefit ratio.**

As of Amendment #04, there will be no additional accrual to the Phase III component of the trial regardless of the outcome of the Phase II analysis and the study will be permanently closed to accrual.

UPDATES TO THE PROTOCOL:

Cover Page

- Drs. Wendy Stock and Geoffrey L. Uy have replaced Dr. Richard M. Stone as the Leukemia Committee Co-Chairs. All contact information has been updated accordingly.
- Dr. Marina Konopleva has replaced Dr. John C. Byrd as the Correlative Study Co-Chair. All contact information has been updated accordingly.
- Dr. Ken Byrd has replaced Dr. Stephen Strickland as the ECOG-ACRIN Study Champion. All contact information has been updated accordingly.
- Dr. Jun (Vivien) Yin's email address has been updated.
- Per the updated Alliance protocol template, the institution names associated with the co-chairs and study champions have been removed.

Study Resources (Page 2)

- Per the updated Alliance protocol template, Ilene Galinsky's institution name and phone number have been removed.
- Caroline Harvey has replaced Ryan Daley has the A041701 Pharmacy Contact. All contact information has been updated accordingly.
- The telephone number for the Alliance Hematologic Malignancy Biorepository (HEME) has been updated.

CTSU Address and Contact Information (Page 3)

This section has been changed to reflect the updated boilerplate language.

Section 4.1 (Investigator and Research Associate Registration with CTEP)

This section has been changed to reflect the updated boilerplate language.

Section 4.2 (Cancer Trials Support Unit Registration Procedures)

This section has been changed to reflect the updated boilerplate language.

Section 4.5 (Patient Registration/Randomization Procedures)

This section has been changed to reflect the updated boilerplate language.

Section 6.1 (Data Collection and Submission)

- This section has been changed to reflect the updated boilerplate language.
- Section 6.1.3 (Data Quality Portal) has been changed to reflect the updated boilerplate language.
- Section 6.1.4 (Rave-CTEP-AERS integration) has been added to reflect the Alliance protocol template

Section 9.1.1 (Rave-CTEP-AERS integration)

This section has been changed to reflect the updated boilerplate language.

Section 13.1.1 (Primary Endpoint)

The following information has been added to the end of the section: "As of Amendment 04, there will be no additional accrual to the Phase III component of the trial regardless of the outcome of the Phase II analysis."

Section 13.1.2 (Sample Size and Power Justification)

The following information has been added to the end of the section: "As of Amendment 04, there will be no additional accrual to the Phase III component of the trial regardless of the outcome of the Phase II analysis."

Section 13.2.1 (Primary Endpoint)

- The first sentence of the Phase II component's final analysis paragraph has been updated to the following: "The Phase II decision-making will be conducted when at least 191 events are observed (approximately expected 37 months after the first patient enrolled). If less than 191 events are observed 2 years after Phase II accrual ends, then the Phase II decision will occur at the target data lock."
- The second sentence of the Phase II component's final analysis paragraph has been moved to be its own paragraph in the "Phase II component" subsection.
- The second paragraph in the "Phase II component" subsection has been updated to the following: "At the final analysis of the Phase II, it will be concluded that the experimental arm regimen is promising ~~and suggest proceeding to the Phase III component of the trial~~, if we a one-sided p-value < 0.10 from the log-rank test ~~observe an HR <= 0.831~~ favoring the experimental arm."
- The following information has been added as a third paragraph in the "Phase II component" subsection: "As of Amendment 04, there will be no additional accrual to the Phase III component of the trial regardless of the outcome of the Phase II analysis. Given the maturity of follow-up on the current patients and no additional accrual to the trial, the final Phase III OS analysis will also be performed at the time of final Phase II EFS analysis. All Phase III alpha (one-sided 2.5%) will be spent at this analysis. The target data lock date is August 12, 2024."
- The first sentence of the Phase II component's interim analysis paragraph has been updated to the following: "We will conduct a futility interim analysis which will take place after 50% of the total events ~~are~~ have occurred (approximately 25 months after the first patient enrolled)."
- The following information has been added after the table as a second paragraph in the "Phase III component" subsection: "As of Amendment 04, there will be no additional accrual to the Phase III component of the trial regardless of the outcome of the Phase II analysis. Given the maturity of follow-up on the current patients and no additional accrual to the trial, the final Phase III OS analysis will also be performed at the time of final Phase II EFS analysis. The final Phase III of analysis of OS will conclude that the novel regimen significantly improves the OS compared to the daunorubicin and cytarabine arm if the one-sided p-value from the stratified log-rank test is < 0.025. The target data lock date is August 12, 2024."

Section 13.3 (Accrual Time and Study Duration)

The following information has been added to the end of the section: "As of Amendment 04, there will be no additional accrual to the Phase III component of the trial regardless of the outcome of the Phase II analysis."

Section 13.5 (Study Monitoring)

The following information has been added to the end of the section: "All EFS and OS outcome data will be requested for release after DSMB review at the time of the final Phase II EFS analysis, with patient follow-up continuing per protocol."

Section 13.7 (Inclusion of Women and Minorities)

This section has been changed to reflect the updated boilerplate language.

Section 14.1.3 (Methods)

- The fifth sentence of the first paragraph has been moved to the second paragraph of the section.
- The second paragraph has been completely revised to list of time points of the samples in a bullet list format.
- The second sentence of the first bullet point under the "Submission of Cytogenetic Samples" subsection to be the following: "Include the karyotype description or clone number in the bottom of the high resolution electronic image ~~(.jpeg or .tiff files)~~ with arrows placed indicating abnormalities."
- After the second sentence of the first bullet point under the "Submission of Cytogenetic Samples" subsection, the following information has been added: "Images (karyotype, metaphase, and FISH) are preferred to be submitted together in one PowerPoint (PPT) file. If this is not possible, individual .jpeg or .tiff files are accepted."
- Under the "Submission of Cytogenetic Samples" subsection, the fourth bullet point has been updated to the following: "If case is abnormal, non-clonal (has one or more of the characteristic abnormalities specified on the list), enter the ISCN of each cell and provide a karyotype and corresponding metaphase representing each type of abnormality present."
- After the first sentence of the seventh bullet point under the "Optional Additional Procedures" subsection, the following information has been added: "Abnormal FISH results are encouraged to be submitted."
- Under the "Optional Additional Procedures" subsection, the third sentence of the seventh bullet point has been updated to the following: "Provide FISH information and two images (in the PowerPoint file with karyotypes and metaphases (preferred) or as individual .jpeg or .tiff files) for each assay performed."
- The heading of the third subsection has been updated to the following: "Questions regarding karyotype submission can be directed to Lisa Sterling, Cytogenetic Data Manager, at"
- Under the "Questions regarding karyotype submission can be directed to Lisa Sterling, Cytogenetic Data Manager, at" subsection, the address for the Alliance Cytogenetics Committee Office has been completely removed.

Section 14.1.4 (Analyses)

The first sentence has been completely removed.

Section 15.0 (Monitoring Plan and Regulatory Considerations)

- The section heading has been updated to the following: "Monitoring Plan and Regulatory Considerations."
- Section 15.3 (Early Study Closure at Sites) has been added to provide guidance regarding early study closure at sites.

UPDATES TO THE MODEL CONSENT:

No changes have been made to the model consent.

Replacement protocol and model consent documents have been issued.

ATTACH TO THE FRONT OF EVERY COPY OF THIS PROTOCOL

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of a study drug, uproleselan, to the usual chemotherapy treatment (daunorubicin and cytarabine) in older adults with acute myeloid leukemia

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: A041701, "A Randomized Phase II/III Study of Conventional Chemotherapy +/- Uproleselan (GMI-1271) in Older Adults with Acute Myeloid Leukemia Receiving Intensive Induction Chemotherapy," (NCT03701308)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have acute myeloid leukemia (AML).

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

This study is conducted by the Alliance for Clinical Trials in Oncology, a national clinical research group supported by the National Cancer Institute. The Alliance is made up of cancer doctors, health professionals, and laboratory researchers, whose goal is to develop better treatments for cancer, to prevent cancer, to reduce side effects from cancer, and to improve the quality of life of cancer patients.

Why is this study being done?

This study is being done to answer the following question:

Can we lower the chance of your AML returning or getting worse by adding a new drug to the usual combination of drugs?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your AML. The usual approach is defined as care most people get for AML.

What is the usual approach to my acute myeloid leukemia?

The usual approach for patients who are not in a study is treatment with the chemotherapy drugs daunorubicin and cytarabine. These chemotherapy drugs are approved by the Food and Drug Administration (FDA). There are two parts to the usual treatment: 1) Remission Induction Therapy and 2) Consolidation Therapy. The goal of Remission Induction is to get rid of as many leukemia cells as possible. Induction is considered successful if remission is achieved. Further treatment is then given to destroy any remaining leukemia cells and help prevent relapse. This is called Consolidation. For patients who get the usual approach for this cancer, about 15 out of 100 are free of cancer after 5 years.

If you have AML with myelodysplastic related changes, another treatment option would be CPX-351 (Vyxeos). Vyxeos has been shown to help patients with this type of AML live longer than treatment with cytarabine and daunorubicin. By enrolling on this study, you will not receive Vyxeos. Another commonly used treatment for AML in older adults who cannot or do not want to receive cytarabine and daunorubicin are hypomethylating drugs like azacitidine or decitabine. Azacitidine and decitabine are less intensive approaches to treat AML, but are not FDA approved for AML, and will not cure the disease.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get the usual treatment (daunorubicin and cytarabine) for up to 5 months, or you will get the usual treatment (daunorubicin and cytarabine) plus the study drug (uproleselan) for up to 5 months.

After you finish your treatment, your doctor will continue to follow your condition and watch you for side effects for up to 5 years after you are registered to the study. You will have clinic visits every 2 months for the first year, every 3 months for the second year, and then every 6 months until 5 years after you are registered to the study. After you finish seeing your doctor, we will collect the results of any of the usual blood or bone marrow tests you have done in the subsequent 5 years to see if your DNA has changed.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not work for you and your AML might get worse. If this happens your doctor will take you off the study and discuss other treatment options with you.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Low blood counts
- Fever and infection
- Nausea and vomiting
- Bleeding

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that both the usual approach and the study approach are effective in the treatment of AML. It is not possible to know now if the study drug/study approach will extend your life or extend your time without disease compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change, risk to your health. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the, Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor the National Cancer Institute (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the usual treatment alone to using uproleselan plus the usual treatment. The addition of uproleselan to the usual treatment could prevent your cancer from returning or getting worse. But, it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if this different approach is better than the usual approach. To decide if it is better, the study doctors will be looking to see if the study approach increases the life of patients by 4 months or more compared to the usual approach.

Uproleselan is not approved by the FDA for treatment of your disease. There will be about 670 people taking part in this study.

What are the study groups?

This study has 2 study groups.

- **Group 1**

  If you are in this group, you will get the usual drugs used to treat this type of cancer (daunorubicin and cytarabine). During Remission Induction therapy, you will get daunorubicin through a vein in the arm on days 1-3 and cytarabine through a vein in the arm on days 1-7. You may be given a second course of Remission Induction therapy if necessary. If the Remission Induction therapy has been effective against your leukemia, you will receive up to 3 cycles of Consolidation therapy, where you will get cytarabine through a vein in the arm on days 1-5 of each 28-day cycle.

  There will be about 335 people in this group.

- **Group 2**

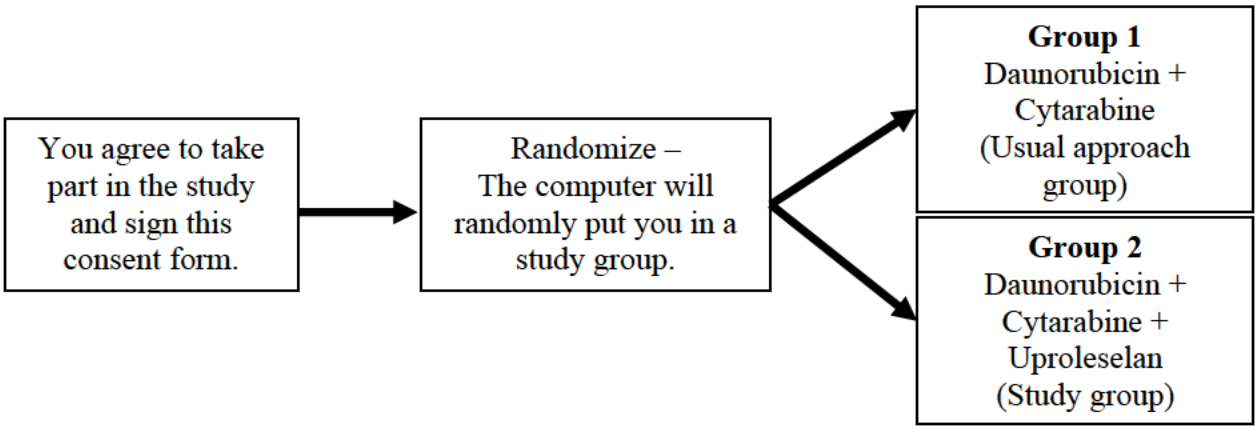
If you are in this group, you will get a study drug called uproleselan plus the usual drugs used to treat this type of cancer (daunorubicin and cytarabine). During Remission Induction therapy, you will get daunorubicin through a vein in the arm on days 2-4, cytarabine through a vein in the arm on days 2-8, and uproleselan through a vein in the arm on days 1-10. You may be given a second course of Remission Induction therapy if necessary. If the Remission Induction therapy has been effective against your leukemia, you will receive up to 3 cycles of Consolidation therapy, where you will get cytarabine through a vein in the arm on days 2-6, and uproleselan through a vein in the arm on days 1-8 of each 28-day cycle.

You will not be able to get additional doses of the drug.

There will be about 335 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

- A bone marrow aspirate sample and a blood sample from a vein in your body will be obtained before you begin study treatment. About 1 teaspoon of bone marrow aspirate and 2 teaspoons of blood will be collected for the study. These samples are required and will be collected at the same time as the other bone marrow and blood samples that are part of the usual treatment for leukemia. You will not need to have an extra bone marrow aspirate procedure for the study.

  These samples will be used for studies that may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems. You and your study doctor will not get reports or other information about any research that is done using your samples.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that the study drug/study approach may not be as good as the usual approach for your AML at preventing your cancer from coming back.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

Bone Marrow Aspirate & Biopsy Risks

There may be some temporary pain or discomfort associated with bone marrow aspirations and biopsies at the site where the needle is inserted. The side effects associated with obtaining bone marrow samples include pain at the site of the procedure, as well as possible bleeding, bruising or swelling. Pain can be treated with regular pain medications. There is also a very small chance that you could develop an infection at the site of the procedure.

Blood Collection Risks

There can be mild pain, or some bleeding or bruising when blood is drawn. Rarely, an infection can happen where the needle was placed. Feeling dizzy or fainting can also happen, but may only last a few minutes after blood is drawn.

Genetic Testing Risks

Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back

to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.

In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

Side Effect Risks

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 and Group 2 – Possible side effects of Daunorubicin or Cytarabine are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

Possible Side Effects of Daunorubicin
(Table Version Date: October 10, 2017)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Daunorubicin, more than 20 and up to 100 may have:
• Pink or red colored urine, sweat, or saliva • Nausea, vomiting • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Daunorubicin, from 4 to 20 may have:
• Damage to the heart which may cause shortness of breath, tiredness • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require transfusion • Pain and sores in mouth and throat • Diarrhea • Redness and pain at the site of previous radiation • Swelling and redness at the site of injection • Loss of nails • Dark discoloration of the nail, skin

RARE, AND SERIOUS In 100 people receiving Daunorubicin, 3 or fewer may have:
• Cancer of the bone marrow (leukemia) caused by chemotherapy • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Possible Side Effects of Cytarabine
(Table Version Date: July 27, 2015)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cytarabine, more than 20 and up to 100 may have:
• Blood clot • Rash • Swelling in the rectum which may cause rectal pain • Diarrhea, loss of appetite, nausea, vomiting • Sores in mouth which may cause difficulty swallowing • Anemia which may cause tiredness, or may require blood transfusions • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cytarabine, from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cytarabine, from 4 to 20 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Numbness and tingling of the arms and legs • Severe blood infection • Kidney damage which may cause swelling, may require dialysis • Headache • Dizziness • Chest pain • Hair loss • Liver damage which may cause yellowing of skin or eyes • Swelling and redness of the eye

RARE, AND SERIOUS In 100 people receiving Cytarabine, 3 or fewer may have:
• Coma

Study Group 2 - In addition to side effects listed above, people who are in Group 2 may also have some side effects from uproleselan. These side effects are listed below.

Possible Side Effects of Uproleselan

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Uproleselan (GMI-1271), from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Heartburn • Reaction during or following a drug infusion which may cause fever, chills, rash, low blood pressure • Bruising, bleeding • Loss of appetite • Pain • Dizziness, headache, tiredness • Changes in taste • Restlessness

Additional Drug Risks

Uproleselan in combination with other drugs could cause risks known to be caused by the other drug to get worse, or the combination may result in risks never previously associated with either drug.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For men: Do not father a baby while taking part in this study. Tell your study doctor right away if you think that your partner has become pregnant during the study or within 3 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the uproleselan ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include the extra bone marrow aspirate and blood collections at the beginning of the study.

If you are in Group 2: You or your insurance provider will not have to pay for the uproleselan while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future.
- The pharmaceutical collaborator, GlycoMimetics
- The IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research.
- The Alliance for Clinical Trials in Oncology

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records

and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

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

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect bone marrow and blood samples for research to measure a protein, E-selectin, and how it interacts with the leukemia in your blood and bone marrow. We will take bone marrow before treatment, at the end of induction, and at the end of consolidation and blood before treatment and at the end of induction to determine the levels before and during treatment. We will use two different techniques, either by measuring proteins in your blood and blood cells to determine if these change during treatment and whether they can predict clinical outcomes. We will also use the bone marrow to look at the levels of certain genes associated with E-selectin to see how they impact clinical outcomes. Researchers will also use these samples to test for levels of leukemia cells in the bone marrow. This is known as Minimal Residual Disease (MRD).

Unknown future studies

If you choose to take part in this optional study, blood and bone marrow samples will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Alliance for Clinical Trials in Oncology and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

We don't know what research may be done in the future using your blood and bone marrow samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes,

piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

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

1. About 4 teaspoons of blood will be collected from a vein in your arm before you begin the study, at the end of induction, at the end of consolidation, and if you were to relapse. About 2 teaspoons of bone marrow aspirate will be collected before you begin the study, at the end of induction, at the end of consolidation, and if you were to relapse. These samples will be collected at the same time as other bone marrow samples that are part of the usual treatment.
2. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.

2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree to have my bone marrow and blood collected, and I agree that my samples and related health information may be used for the laboratory study described above.

1) YES NO

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from this study.

2) YES NO

Samples for unknown future studies:

I agree to have my bone marrow and blood collected, and I agree that my samples and related health information may be kept in a biobank for use in future health research.

3) YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

4) YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature