KEY INFORMATION FOR METABOLICALLY OPTIMIZED, NON-CYTOTOXIC LOW DOSE WEEKLY DECITABINE/VENETOCLAX IN MDS AND AML

We invite you to take part in a research study because you have either myelodysplastic syndrome (MDS), Acute Myeloid Leukemia (AML), or a related cancer. This study will involve two drugs called decitabine and venetoclax. Decitabine is FDA approved for treatment of MDS and AML. Venetoclax is approved for AML in combination with Azacitidine for patients with AML or are over age 75 or unfit for chemotherapy. In this study, decitabine and venetoclax will be administered using a low dose weekly schedule in an attempt to improve their effectiveness by decreasing the side effects that often occur when they are given at standard dosing.

This page is designed to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The treatment with decitabine and venetoclax will continue as long as the therapy is helping you. The purpose of this research is to gather information on the safety and effectiveness of decitabine and venetoclax.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

We cannot know if you will have any benefit as a result of your participation in the study; it is possible the study treatment may improve your bone marrow condition, which may give you relief from some symptoms, improve your quality of life or prolong your survival. However, it is possible that your condition could worsen. Your participation in this study will help to obtain information about treating subjects with bone marrow failure, leukemia and related cancers.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

The medications 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 be testing your blood and will let you know if changes occur that may affect your health. *For a complete description of risks, refer to the Consent Document.*

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights or access to care you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Mendel Goldfinger If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his phone number is: 718-920-4826.

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Einstein Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 718-430-2253 or irb@einsteinmed.edu

ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

Introduction

You are being asked to be a subject in a research study called **Metabolically Optimized, Non-cytotoxic Low Dose Weekly Decitabine/Venetoclax in MDS and AML.** Your participation is voluntary -- it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." His name is Dr. Mendel Goldfinger. You can reach Dr. Goldfinger at:
Office Address: 111 East 210 street
Bronx, NY 10467
Telephone #: 718-920-4826
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einsteinmed.edu, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

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Why is this study being done?

Diseases like AML and MDS are cancers of the bone marrow which lead to bone marrow failure. The bone marrow is the place in the body where components of blood such as red cells, platelets and white cells are made. Bone marrow failure is the result of abnormalities that prevent bone marrow cells from developing into red blood cells, white blood cells and platelets.
DNA is a chemical substance within cells that stores information needed for cell growth and cell behavior. One approach to treating the malignant cells is to give chemotherapy which damages DNA within these cells and causes their death. Unfortunately, such therapy has side-effects, since normal cells can be affected by the treatment.

Decitabine is approved by the US Food and Drug Administration for treatment of MDS and AML. Venetoclax is approved for AML in combination with azacitidine for patients with AML or are over age 75 or cannot receive other chemotherapy. In this study, decitabine and venetoclax will be administered using a different dosing and schedule than the approved dosing and schedule. This study is using a low dose weekly schedule of

decitabine and venetoclax in an attempt to improve efficacy by decreasing the side effects often seen when these drugs are given at standard dosing.

Why am I being asked to participate?
We are asking you to be a subject in a research study because you have either myelodysplastic syndrome (MDS), Acute Myeloid Leukemia (AML), or a related cancer.

How many people will take part in the research study?
All study participants will receive decitabine and venetoclax.

There are atotal of 3 sites (including Montefiore Einstein Comprehensive Caner Center) participating on this trial.
In the initial safety and tolerability phase of the study, 33 patients will be enrolled. In the second expansion phase of the study up to 85 patients (including from the 1st stage), will be enrolled.

How long will I take part in this research?
The treatment with decitabine and venetoclax will continue as long as the therapy is helping you. This can be weeks, months, or maybe even years.

What will happen if I participate in the study?

Before You Receive Study Medications:
You will need to have certain exams, tests or procedures before getting any study treatment. They are done to make sure that it is safe to give you the study medications. Some of these exams, tests or procedures are part of regular bone marrow failure care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. If they were done too long ago they may need to be repeated. Your doctor/study team will discuss which, if any, tests need to be repeated. You will not receive any study treatment during this time.

During The Study
If the exams, tests, and procedures show that you can be in the study, and you choose to take part, then you will have the following tests and procedures done.

You will need these tests and procedures that are part of regular care.

- You will have to come to the clinic on days 1,8,15,22 (for aggressive disease decitabine will be added on days 2,9,16,23) of 28 day cycle to receive your injection of decitabine treatment. The dose of decitabine is based on how much you weigh; the study staff will tell you your dose if you want to know it. You will also be taking venetoclax at a dose of 400 mg orally on day 1,8,15,22 of 28 day cycle. (The doses of both may be changed, based on how you are responding to them, by other medications that you are taking, and by side effects.)
- During the first 12 weeks of treatment, you will have blood counts done every week. About 15 ccs of blood, or about a tablespoon, will be drawn to assess your need

for transfusions, routine kidney and liver tests, the status of the MDS or AML, and to monitor for side effects of the treatment. After the first 12 weeks, these will be done every 2 weeks unless your doctor thinks it is safer to continue to check the blood counts more frequently.

- You will have short interviews and physical examinations to assess your health and well-being.
- Every 12 weeks, you will undergo bone marrow aspirates and biopsies) so that we can look at your bone marrow under the microscope for improvement or worsening of the MDS or AML, and perform standard tests for chromosome abnormalities that are a feature of bone marrow failure. These results will be used to make any needed adjustments to the treatment.

End of Study

You can decide to stop being in the study at any time. Tell the study doctor if you are thinking about stopping or decide to stop. It is important that you tell your doctor, so he or she can:

- Tell you how to stop safely, since there are times during the study when it would be very unsafe for you to withdraw.
- Talk to you about what follow-up care and testing could be most helpful for you.

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.

What is the usual approach to my myelodysplastic syndrome (MDS) and Acute Myelogenous Leukemia (AML)?

Treatments may include supportive care, drug therapy with chemotherapy, and stem cell transplantation. Supportive care may include blood transfusions, medications to increase the making of red blood cells, and antibiotics. Drug therapy may include the medication azacitidine, decitabine, venetoclax. Certain people can be cured with chemotherapy followed by a stem-cell transplant from a donor.

Genetic Testing

This study will not involve genetic research or genetic testing be stored for future research studies.

Specimen Banking (Future Use and Storage)

If you agree, we will store your specimens and information about you in a “biobank”, which is a library of information and specimens (tissue and blood) from many studies. These specimens and information can be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose or treat disease, including genetic research. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained

by the federal government. Your specimens and information may be kept for a long time, perhaps longer than 50 years. You may remove your consent for future research at any time by contacting the Principal Investigator named on the first page of the consent or the IRB office at 718-430-2237. If you do, we will destroy remaining specimens and information but if these were already shared with other researchers, we cannot get them back.

You can choose not to participate in the biobank and still be part of the rest of the study and this will not affect your treatment at this facility**.**

INITIAL ONE (1) OF THE FOLLOWING OPTIONS
_____ I consent to have my specimens and information about me used for future research studies.
_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

INITIAL YOUR CHOICE BELOW
_____ I consent to be contacted in the future to learn about:
_____ New research protocols that I may wish to join.
_____ General information about research findings.
_____ I do not want to be contacted at all.

Will I be paid for being in this research study?
You will not receive any payment or other compensation for taking part in this study.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?
Neither you nor your insurance provider will be responsible for the costs of any research-only tests or procedures. The tests that are for research purposes will not be charged to you and will be paid for by the research study.

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your MDS or AML in this study (i.e., the medications, medical history, review of medications, physical exams, performance status, routine blood tests, pregnancy test, as well as, the costs associated with the administration of the drug, facility fees, etc.). Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

Conflict Of Interest Disclosure:
Marina Konopleva, MD, one of the doctors (Sub-Investigator) involved in this study, receives compensation from Abbvie, The compensation, Dr. Konopleva receives from Abbvie is for work as an advisor.
Abbvie is the manufacturer and marketer of the Venetoclax – an investigational drug used in this study.

What will happen if I am injured because I took part in this study?
If you are injured as a result of this research, only immediate, essential, short-term medical treatment as determined by the participating hospital, will be available for the injury without charge to you personally.

- No monetary compensation will be offered.
- You are not waiving any of your legal rights by signing this informed consent document.
- If additional treatment is required as a result of a physical injury related to the research, necessary medical treatment will be provided to you and billed to your insurance company or to you as part of your medical expenses.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Dr. Goldfinger at (718) 920-4826.

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including "over-the-counter" remedies and nutritional supplements or herbs.
- You must take your study drug as instructed, returning any unused study drug (including any empty bottles), at every visit.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- ***Drugs may cause a reaction that, if not treated promptly, could be life-threatening. It is important that you report all symptoms, reactions and other complaints to the research study doctor.***
- If you think you have become pregnant, contact your research study doctor immediately.
- If any other doctor recommends that you take any medicine, please inform him/her that you are taking part in a research study. You should give the other doctor the research study doctor's name and phone number.
- You may carry out all your normal daily activities.

Confidentiality
The researchers and study staff follow federal and state laws to protect your privacy. This part of the consent form tells you what information about you may be used and shared in the research described in this form. You do not have to sign this form but, if you do not, you may not participate in the research.

The health information that we may use or disclose for the research described in this form includes information from your entire medical record, such as your name, phone number, email, medical diagnoses, dates, test results, social security number, medical record numbers, etc.
Your information and research records will be kept confidential. Your study information will be kept as long as they are useful for the research described in this form.

The only people who can see your research records are:

- Researchers and other individuals who work with the researchers
- Organizations and institutions involved in this research, including those that fund the research, if applicable
- Groups that review research such as central reviewers, Institutional Review Boards, the Office for Human Research Protections, the US Food and Drug Administration, data coordinating centers, and domestic and foreign agencies that regulate research.

The purposes of these uses and disclosures are to (1) conduct the study and (2) make sure the study is being done correctly. The information covered under this form may no longer be protected by federal privacy laws (such as HIPAA) once disclosed, and those persons who receive your health information may share your information with others without your additional permission. All of these groups have been asked to keep your information confidential.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

To maintain the integrity of this research study, you generally will not have access to your research-related personal health information. If it is necessary for your care, your research-related health information will be provided to you or your physician.

Are there any risks to me?

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

If you choose to take part in this study, there is a risk that:

- The study drug/study approach may not be better, and could possibly be worse, that the usual approach for your disease.
- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss.
- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with 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. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

The medications used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The most common side effects with decitabine and venetoclax are worsening of blood counts. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.
Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.

As with any experimental treatment, there may be adverse events or side effects that are known or are currently unknown. Some of these unknown risks could be permanent, severe, or life-threatening. Your health care team may give you medicines to help lessen side effects. Side effects can be serious. Side effects can be long lasting. Side effects may never go away.

Tell the study doctor or research team as soon as possible if any of the side effects, risks or discomforts listed below occur or if you think a side effect that is not listed may be happening.

If your condition worsens, if side effects become very severe, or if it turns out that being in this study is not in your best interest, you will be taken out of the study.

If questions come up about side effects, ask the study doctor or staff at any time during or after the study.

Risks or discomforts of the study medications

<u>Venetoclax side effects:</u>

- Lowering of white blood cell, platelet, and red blood cell counts (these are the types of cells that are in blood): If the white blood cell is too low, it increases the risk of

certain types of infection. If the platelet count is too low, it increases the risk of abnormal bleeding. If the red blood cell count is too low, it may cause fatigue, shortness of breath, or heart failure. With lowering of blood counts you may need transfusions of red blood cells and/or platelets.

- Gastrointestinal side effects: Nausea, diarrhea, constipation, abdominal pain, decreased appetite and vomiting
- Kidney failure, which may cause your body to not filter toxins effectively or produce enough urine.
- Inflammation of the liver, which may cause abdominal pain or jaundice (yellowing of the skin or eyes).
- Increase in potassium levels in the bloodstream, which may lead to palpitations or abnormal heart rhythms and require treatment with medications.
- Lowering of calcium levels in the bloodstream, which may cause muscle cramps, weakness, or seizures, and require treatment with medications.
- Lowering of sodium levels in the bloodstream, which may cause nausea, headache, confusion, and weakness, and require treatment with medications.
- Bone pain
- Headache
- Rash
- Fatigue
- Infections

Decitabine side effects:

- Lowering of blood counts: see the earlier comments in the previous paragraph, on the side effects of venetoclax. Decitabine can have the same side effects.
- Gastrointestinal side effects: Nausea, diarrhea, constipation, abdominal pain, decreased appetite and vomiting
- Fluid retention
- Muscle and joint pain
- Headache
- Dizziness

Blood draws

The insertion of the needle to draw blood is painful; however, the discomfort is usually brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

Bone marrow aspiration and biopsy

There are also risks associated with taking samples of your bone marrow. Your study doctor or his/her designee will insert a needle into your hip to withdraw a sample of fluid containing bone marrow cells. The risks of bone marrow sampling commonly include discomfort, pain, redness, swelling, and/or bruising where the sample is taken from your hip. Sometimes bleeding can occur at the place where the sample is drawn. Fainting and infection can happen, but rarely. Many patients also experience soreness or stiffness in the hips for several days after the procedure. You may feel a mild to moderate degree of

pain or discomfort during the procedure. Your study doctor will discuss with you if you need an anesthetic to manage the pain associated with the repetitive biopsies during the study.

Reproductive risks

You should not get pregnant, breastfeed, or father a baby while in this study. The medications used in this study could be very damaging to an unborn baby. The study doctor will discuss the types of birth control, or pregnancy prevention, to use while in this study.

Pregnant women or women who are breast feeding will not be enrolled in this study because we do not know what effect the study medications will have on an unborn child. If applicable you must stop breast feeding if you receive study treatment. If you are a woman capable of having children, you will be given a pregnancy test before you begin the study, which must be negative in order for you to take part.

Women

If you are a woman capable of having children and choose to have sex, you must use two forms of acceptable contraception, including one barrier method (e.g. latex condom, diaphragm or cervical/vault cap when used with spermicidal foam/gel/cream/film/suppository), while you are in this study and for 4 weeks after you receive the study treatment. One of the acceptable methods of contraception is the use of a condom along with a diaphragm with spermicidal agent (foam/gel/cream/film/suppository).

Additional methods are:

- IUD or IUS (intrauterine devices or intrauterine system, except IUD progesterone T) in addition to a barrier method with spermicide.
- Prior vasectomy by any male partner.
- Use of approved oral, injected, or implanted hormonal methods of contraception in addition to a barrier method with spermicide. This must be approved by your study doctor before you begin taking the study drug.

Even if you use birth control during the study, there is still a chance you could become pregnant. If you become pregnant or you think you may be pregnant during the study, you must immediately tell your study doctor. If you become pregnant during the study, the pregnancy will be followed to determine the outcome. If you become pregnant during the study, the study treatment may involve unforeseeable risks to the unborn baby.

Men

Men who are able to father children must use adequate contraception. If you are a man you must:

- Prevent pregnancy in a female partner.
- Prevent exposure of a partner to semen by any means (not just intercourse).
- You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, she should promptly notify her doctor.

You should not donate sperm for 4 weeks after your last dose of study treatment. In addition, acceptable methods of birth control include using one of the following while you are in this study and for 4 weeks after your last dose of the study treatment (due to the unknown effects of the study treatment on the sperm):

- Abstinence (no sex)
- Condom plus spermicidal agent (foam/gel/cream/film/suppository)
- Prior vasectomy

Are there possible benefits to me?

We cannot know if you will have any benefit as a result of your participation in the study; it is possible the study treatment may improve your bone marrow condition, which may give you relief from some symptoms, improve your quality of life or prolong your survival. However, it is possible that your condition could worsen. Your participation in this study will help to obtain information about treating subjects with bone marrow failure, leukemia and related cancers.

What choices do I have other than participating in this study?

You can refuse to participate in the study. If you decide not to participate, the medical care providers at this facility will still give you all of the standard care and treatment that is appropriate for you.

If you do not wish to take part in this research study, your study doctor will discuss alternate treatment options with you, including their benefits and risks. These may include:

- Getting treatment without being in a study.
- Taking part in other investigational studies if they are available.
- Getting comfort care, also called palliative care, for your symptoms. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. Comfort care tries to keep you as active and comfortable as possible.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated at this facility. However, some of the information may have already been entered into the study and that will not be removed. The researchers may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and he will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

If you decide to stop taking part in the study for any reason, we will ask you to make a final study visit. You will need to return all unused study drug at this visit.

Can the study end my participation early?

We will not let you participate in the study anymore if:

- If your health changes and remaining in the study is no longer in your best interest
- If new information becomes available that indicates you are no longer likely to benefit or are more likely to have serious side effects than expected
- If you do not follow the study requirements

In addition, your participation will end if the investigator or study sponsor stops the study earlier than expected.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	

Printed name of the person conducting the consent process	Signature	Date	