Official Title:	**Salsalate + Venetoclax/Decitabine for Patients with Acute Myelogenous Leukemia or Advanced Myelodysplasia/Myeloproliferative Disease**
NCT number:	**NCT04146038**
Document Type:	**Consent Form: Main**
Date of the Document:	**09/20/2019**

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CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: Salsalate + Venetoclax/Decitabine for Patients with Advanced Myeloid Malignancies
Principal Investigator: [redacted]

STUDY SUMMARY: This consent form is part of an informed consent process for a research study and it will provide information that will help you decide whether you want to take part in this study. It is your choice to take part or not. The purpose of the research is to: is to determine if the addition of a medicine called salsalate to standard medications used to treat patients with acute myelogenous leukemia or related diseases such as myelodysplasia or myeloproliferative diseases will result in additional side effects compared to the standard therapy alone. If you take part in the research, you will be asked to have a bone marrow biopsy before starting therapy and after the second course of therapy. You will also have blood tests, sometimes daily. If your blood cell count is above that threshold you will receive chemotherapy to lower the blood counts to a safe level. The study medication, salsalate will be taken as 2 pills twice a day for 7-10 days. The standard component of the treatment includes chemotherapy (decitabine or 5-azacytidine) administered over 1h for 7-10 days for the first cycle. Venetoclax will be administered as 1-4 pills/day (depending upon other medications being taken) continuously unless interrupted by your physician for medical reasons. Your time in the study will take generally 1 month. Patients enrolled in the clinical trial will receive experimental therapy for only the first course of therapy. If the treatment appears to be controlling the disease, you will then continue on treatment with decitabine (or 5-azacytidine) in combination with venetoclax as standard therapy. Possible harms or burdens of taking part in the study may be infection, bleeding, fatigue, fever, low platelet counts, damage to the kidneys, allergic reactions, nausea, and hearing abnormalities, and possible benefits of taking part may be more people entering remission and longer durations of remission. An alternative to taking part in the research study is no treatment or standard decitabine (or 5-azacytidine) in combination with venetoclax; or intensive induction chemotherapy. The data collected will be how well the new combination of medications is tolerated and whether the combination alters the biological characteristics of the leukemia cells. We will also determine if the combination is effective in treating the blood disorder (leukemia, myelodysplasia or related disease). Your alternative to taking part in the research study is not to take part in it and receive standard therapy.

The information in this consent form will provide more details about the research study and what will be asked of you if you choose to take part in it. If you have any questions now or during the study, if you choose to take part, you should feel free to ask them and should expect to be given answers you completely understand. After all of your questions have been answered and you wish to take part in the research study, you will be asked to sign this consent form. You are not giving up any of your legal rights by agreeing to take part in this research or by signing this consent form.

Who is conducting this research study?

[redacted]

Expiration Date: 5/14/2022

[redacted]

The Principal investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

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Why is this study being done?
The purpose if this study is to determine if the addition of a medicine called salsalate to standard medications used to treat patients with acute myelogenous leukemia or related diseases such as myelodysplasia or myeloproliferative diseases will result in additional side effects compared to the standard therapy alone. Salsalate is not approved by the FDA. Use of Salsalate to treat patients with acute myelogenous leukemia (AML), myelodysplasia (MDS) or related diseases is experimental. This study is being done because it is hoped that salsalate will enhance the beneficial effects of decitabine (or 5-azacytidine) and the treatment will result in more people entering remission and having longer durations of remission.

Who may take part in this study and who may not?
Any patient over the age of 18 who has acute myelogenous leukemia (AML) or advanced myelodysplasia (MDS) or myeloproliferative disease (MPD) may take part in this study if they are not a candidate for aggressive chemotherapy. You may not take part in the study if you have certain concurrent illnesses or laboratory values that make the study treatment likely to cause too many side effects. The study doctor and/or research team will also ask you other questions about your medical history in order to make sure you qualify to be in this study. A component of this study uses standard treatment with decitabine (or the related medication 5-azactidine) in combination with venetoclax. These cost of these drugs are not covered by the clinical trial. If your insurance does not cover the cost of these drugs (or the co-pay is too high) you will not be able to participate in the clinical study.

Why have I been asked to take part in this study?
You have been asked to participate in this study because you have acute myelogenous leukemia (AML) or another related cancer that is in advanced stage as judged by blood or bone marrow tests. The related disease may be called myelodysplasia (MDS), chronic myelomonocytic leukemia (CMML) or a myeloproliferative disease (MPD). Your doctors believe that the best treatment for you is with a chemotherapy agent called decitabine (or the related medication 5-azactidine) in combination with a medication called venetoclax. This combination is new treatment modality that has recently been approved by the Food and Drug Administration for patients with AML who are not considered likely to get benefit from (or who have medical problems that preclude) intensive chemotherapy. These patients may be older, have concurrent

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medical issues, or have disease characteristics that make them unlikely to have durable benefit from intensive chemotherapy.

Research done at Rutgers CINJ have shown that an anti-inflammatory medicine in the family of medicines called salicylates may improve the results of the combination of decitabine (or the related medication 5-azacytidine) and venetoclax. In this study we will treat 20 patients with a salicylate called salsalate in addition to decitabine (or the related medication 5-azactidine) in combination with venetoclax. We will determine the side effect profile to determine if the salsalate causes any additional side effects. We will also do some tests on your blood cells to see the biological effects of the salsalate.

How long will the study take and how many subjects will take part?
Patients enrolled in the clinical trial will receive experimental therapy for 1 course of therapy (generally 1 month). They will then continue on treatment with decitabine (or 5-azacytidine) in combination with venetoclax as standard therapy until disease progression or other reason for discontinuing therapy. They will be monitored for the duration of therapy with decitabine (or 5-azacytidine) in combination with venetoclax

A total of 20 subjects will be enrolled study wide. All subjects will take part in this study from the Rutgers CINJ.

What will I be asked to do if I take part in this study?
If you take part in this research study you will have a bone marrow biopsy before starting therapy and after the second course of therapy, usually at 2 months. There may be earlier bone marrow tests if your doctor thinks the test is needed to guide your treatment. You will also have blood tests, sometimes daily, as part of standard of care. As part of the study there will be an additional 2 tubes (3 teaspoonfuls) of blood taken before starting therapy and 1-2 days later and 2-4 days later. The safety of decitabine (or 5-azacytidine) in combination with venetoclax is greatest if given when the total number of leukemia cells in the blood is below a certain level. If your blood cell count is above that level you will receive chemotherapy (pills) to lower the blood counts to a safe level. The study medication, salsalate will be taken as 2 pills twice a day for 7-10 days. The treatment also includes chemotherapy (decitabine or 5-azacytidine) administered over 1h for 7-10 days and venetoclax for 28 days, given as 1-4 pills/day (depending upon other medications being taken) for 28 days. The venetoclax may be interrupted by your physician for medical reasons.

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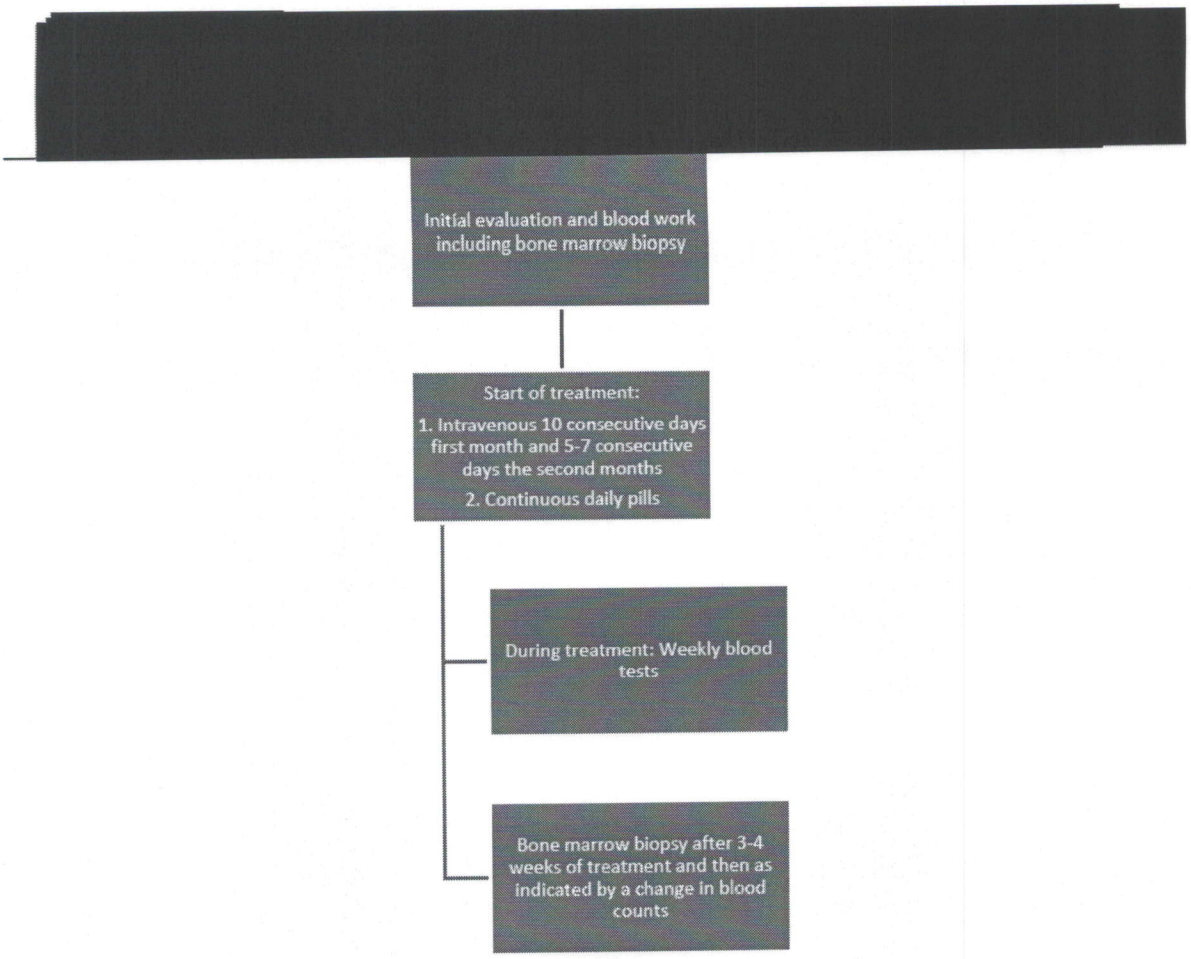

What are the risks and/or discomforts I might experience if I take part in this study?
AML, MDS and MPD are life-threatening diseases. Patients with these diseases often have very abnormal blood counts. The average age of patients with these diseases is over 65 years old and many may have other serious illnesses. Patients with these diseases and abnormal blood counts are very susceptible to infection, bleeding and fatigue. Any treatment for these diseases can make things even worse because blood counts may get worse as a result of the treatment. In prior studies with decitabine or 5-azacytidine in combination with venetoclax serious side effects included fever in almost one half (50%) of the patients, low platelet counts and bleeding occurred in one quarter (25%) of the patients, and serious infections occurred in one quarter (25%) of the patients. Other potential side effects include serious damage to your kidneys from a break down of cancer cells called tumor lysis syndrome. Tumor lysis syndrome can be irreversible, resulting in multiple blood abnormalities, kidney failure and even death. Venetoclax in combination with decitabine or 5-azacytidine has also been associated with nausea, diarrhea, vomiting, fever, rash, bleeding, infection, muscle pain and fatigue. A low platelet count and white blood cell count, which can cause bleeding and infection is common. Side effects directly related to salsalate include damage to the kidneys, allergic reactions, nausea, bleeding and hearing abnormalities as well as dizziness, liver abnormalities, abnormalities, abdominal pain, nausea, diarrhea, edema and somnolence. Some people taking salsalate for more than 3 months have developed heart disease. You will be monitored for these side effects. It is unknown if salsalate will have other unanticipated side effects or increase the side effects of decitabine (or 5-azacytidine) in combination with venetoclax. In general, AML, MDS and MPD are life-threatening diseases with high risk of infec

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and damage to the organs. Every treatment can increase these toxicities and result in infections; bleeding; damage to the heart, lung, kidney, liver, gastrointestinal tract, nerves and/or other organs. Sometimes these toxicities will be irreversible and may result in death. One patient treated with the combination of decitabine, venetoclax and salsalate had serious bleeding. Since then the study has been modified to make sure all patients receive a medicine that reduces production of acid in the stomach. It is hoped that this will reduce the risk of stomach irritation and bleeding.

Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Therefore, your genetic information potentially could be used in ways that could cause you or your family economic stress.

There are state and federal laws that protect against genetic discrimination. A federal law, the Genetic Information Nondiscrimination Act 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: (1) health insurance companies and group health plans may not request your genetic information that we get from this research; (2) health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums; and (3) employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

REPRODUCTIVE RISKS

Both males and females will be included in this study. If you are pregnant, you cannot participate in this study. You should not become pregnant or father a baby while participating in this study because the drugs in this study can be associated with unknown risks that could affect you or an unborn baby.

All subjects and their spouses or partners must use an effective birth control method. Some examples of birth control are the following: have had a prior history of surgically-induced sterility (i.e., tubes tied, vasectomy), avoiding any activity that could cause you to become pregnant (no sexual intercourse), or using birth control pills, IUD, condom, or double-barrier contraception diaphragm with spermicidal jelly, transdermal (through your skin) or injectable contraceptives.

Whether you are a man or woman, you must practice birth control during the study and for at least six months after you receive the last dose of the study drug. Before entering the study, you and the study doctor must agree on the birth control method you will use during the entire study.

A counselor and more information about preventing pregnancy will be made available to you if you have any questions.

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If you are capable of becoming pregnant, a pregnancy test (using a urine and/or blood sample) will be done and the results must be negative before you are permitted to enroll in this study. A repeat pregnancy test must be done if you miss any periods or your menstrual cycle becomes irregular.

If you are currently breast feeding a child and agree to participate in this study, you must stop breast feeding before receiving the first dose of study drug. You must agree to discontinue breast feeding for the entire time you are participating in the study to prevent any potential health risk or injury to the child.

If you become pregnant while in this study, you must tell the study doctor as soon as possible. The study doctor will advise you of the possible risks to your unborn child and options available to you. Because of the possible risks to an unborn child, the study drug will be stopped. You may be asked to receive medical follow-up services for yourself during the pregnancy and for the baby after birth. You may be asked to provide more information about the pregnancy and its outcome.

MALES

Male subjects must be surgically sterile or agree to use an acceptable method of contraception.

You should make certain that you use adequate birth control measures to protect your spouse/female sexual partner(s), who may be capable of becoming pregnant.

You should also make certain that you inform your spouse/female sexual partner(s), who are capable of becoming pregnant, about the risk of harm to an unborn child posed by this drug so that they can take their own contraceptive measures.

Are there any benefits to me if I choose to take part in this study?

There may or may not be direct medical benefit to you from taking part in this study. It is hoped that salsalate will enhance the beneficial effects of decitabine (or 5-azacytidine) and the treatment will result in more people entering remission and longer durations of remission.

What are my alternatives if I do not want to take part in this study?

The following alternative treatments are available if you choose not to take part in this study:

No treatment; standard decitabine (or 5-azacytidine) in combination with venetoclax; or intensive induction chemotherapy.

Talk to your doctor about your choices before you decide if you will take part in this study. You are under no obligation to take part in this research study. If you decide that you do not wish to take part in this study, you are free to leave the study at any time.

How will I know if new information is learned that may affect whether I am willing to stay in the study?

During the course of the study, you will be updated about any new information that may affect whether you are willing to go on taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be [redacted]

[redacted]

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Will I receive the results of the research?
In general, we will not give you any individual results from the study. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence. Life threatening findings on laboratory specimens such as severely low blood counts will prompt expedited notification. You will be notified via phone.

Will there be any cost to me to take part in this study?
You and/or your insurance company will be billed for the costs of your treatment that are considered standard of care (for example, doctor/ Advanced Practice Nurse (APN) visits, nursing care to administer the treatments, routine lab tests, restaging scans, etc.), standard dose decitabine (or 5-azacytidine) and venetoclax as you would have received these services even if you were not participating in this study. You will be responsible for any co-payments due for office visits, co-insurances and deductibles due on any tests and/or procedures that are required and considered standard care. Salsalate will be paid for by the study (CINJ via philanthropic funds).

If you have any questions about insurance coverage, including any out of pocket expenses you might incur, or which laboratory or facilities you are allowed to have tests at, a financial counselor will be made available to you upon request.

Optional and/or research related items such as salsalate, special laboratory tests and research blood samples will be paid for by the [redacted].

Will I be paid to take part in this study?
You will not be paid for your participation in this research study.

How will information about me be kept private or confidential?
All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed.

[redacted] screens containing personal health identifiers are inaccessible to public view. Only the study doctor and research team will have direct access.

What will happen to my information or biospecimens collected for this research after the study is over?
After information that could identify you has been removed, de-identified collected for this research may be used by or distributed to investigators for other research without obtaining additional informed consent from you.

What will happen if I am injured during this study?
If you take part in this study, you will be exposed to certain risks of physical personal injury in addition to those associated with standard forms of treatment.

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that result in personal injury may be discovered. Please refer to section 'What are the risks and/or discomforts you might experience if you take part in this study?".

The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

What will happen if I do not wish to take part in the study or if I later decide not to stay in the study?
It is your choice whether to take part in the research. You may choose to take part, not to take part or you may change your mind and withdraw from the study at any time.

If you do not want to enter the study or decide to stop taking part, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to [redacted]

If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can I call if I have questions?
If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study doctor:

[redacted]

If you have any questions about your rights as a research subject, you can call:

[redacted]

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

[redacted]

[redacted]

[redacted]

The next few paragraphs tell you about how investigators want to use and share identifiable health information from your medical record in this research. Your information will only be used as described here or as allowed or required by law. If you sign this consent form, you agree to let the investigators use your identifiable health information in the research and share it with others as described below. Ask questions if there is something you do not understand.

What is the purpose of the research and how will my information be used?
You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help investigators answer the questions that are being asked in the research.

What information about me will be used?
Your health information related to this study may be used or disclosed in connection with this research study, including, but not limited to, information in your medical record such as certain information indicating or relating to a particular medical condition, blood and other tissue samples and related records, physical examinations, x-rays, MRI's, etc. Your personal identity, that is your name, address, and other identifiers, will be kept confidential. You will have a code number and your actual name will not be used. Only your study doctor will be able to link the code number to your name.

Your data may be used in scientific publications. If the findings from the study are published, you will not be identified by name. Your identity will be kept confidential. The exception to this rule will be when there is a court order or when a law exists requiring the study doctor to report communicable diseases. In this case, you will be informed of the intent to disclose this information to the state agency. Such a law exists in New Jersey for diseases such as cancer, infectious diseases such as hepatitis, HIV, viruses and many others.

In applications for marketing authorization your data may be submitted to domestic and foreign drug regulatory agencies.

Your data may also be sent to domestic and foreign drug regulatory agencies if you should suffer a bad reaction to the study drug.

Who may use, share or receive my information?
The following parties are authorized to use and/or disclose your health information in connection with this research study:

- [redacted]

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

[redacted]
[redacted]

[redacted]

- U.S. Food and Drug Administration (FDA)
- The Office for Human Research Protections (OHRP) in the U.S. Department of Health and Human Services (DHHS)

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my research record while the research is ongoing?
No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I have to give my permission?
No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my permission later?
Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him or her of your decision:

[redacted]

How long will my permission last?
There is no set date at which your authorization will expire. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

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Expiration Date: 5/14/2022

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AGREEMENT TO PARTICIPATE

1. Subject consent:

I have read this entire consent form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form and this study have been answered. I agree to take part in this study.

Subject Name:_____

Subject Signature:_____ Date:_____

2. Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed all the important details about the study including all of the information contained in this consent form.

Investigator/Person Obtaining Consent (printed name):_____

Signature:_____ Date: _____

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