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Masonic Cancer Center
University of Minnesota

CONSENT TO PARTICIPATE IN RESEARCH

Nivolumab, Oral Cyclophosphamide, and N-803 for Relapsed/Refractory Acute Myeloid Leukemia (AML) and Higher-Risk Myelodysplastic Syndrome (MDS)

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For questions about research appointments, the research study, research results, or other concerns, call the study team at:

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This Study is Supported by: Bristol-Myers Squibb Company is supplying the drugs nivolumab and oral cyclophosphamide, and NANTCell Inc (ImmunityBio) is supplying the drug N-803, free of cost for this study.

What is Research:
Doctors and researchers are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to answer one or more questions about a new treatment approach to learn if it is safe and effective. Researchers learn things by following the same treatment plan (or protocol) with a number of participants. You, as an individual, may or may not be helped by volunteering for a research study; however, your participation helps answer the research question(s). Often one or more of the drugs offered on a research study are only available on a research study.
- The goal of routine (standard) treatment is to treat your disease or to improve your quality of life using drugs and other methods that have been proven (often through previous research studies). Standard treatments are available from any cancer doctor. Research and clinical care are often combined. One purpose of this consent document is to provide clear information about specific research activities of this study.

If your doctor is also the person responsible for this research study, please note that he/she is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

What you should know about a research study:

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can ask all the questions you want before you decide.
- You will be given a copy of this consent form.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

Why you are invited to take part in this research study:

You are invited to take part in this research study because you have relapsed (recurrent after treatment) or refractory (did not respond to treatment) Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS) and treatment is recommended.

Why this research is being done:

After failing chemotherapy, the chances of controlling leukemia and MDS with additional chemotherapy are small.

This study is testing a different treatment approach by adding two immunotherapy drugs, nivolumab and N-803, to a chemotherapy drug, cyclophosphamide. Treatment in this study is given as an outpatient.

Nivolumab is a type of immunotherapy. It works by turning on the body's own immune system to attack cancer cells. It is approved by the US Food and Drug Administration (FDA) for the treatment of some types of cancer including melanoma (skin) and lung cancer. Researchers are now testing immunotherapy drugs including nivolumab in blood cancers such as leukemia and MDS.

N-803 is an agent which is a super agonist of Interleukin-15 (IL-15). This agent was developed by Altor BioScience Corporation where it was known as ALT-803. It was renamed N-803 after it was acquired by Nant. Super agonist is a general term given to any drug or agent that is capable of producing greater response than the drug it is based on. IL-15 is a cytokine (a type of protein), which is naturally occurring in humans. The man-made (recombinant) version of IL-15 can stimulate the immune system for the treatment of several types of cancer. However, IL-15 requires daily dosing, ideally as a continuous infusion to be effective. Its administration is inconvenient and expensive. As a super agonist of IL-15, N-803 is being tested as a once every 3 week subcutaneous injection. N-803 is an investigational drug that is not approved by the Food and Drug Administration (FDA); however, this study is being conducted with the FDA's permission.

Cyclophosphamide is most commonly used intravenously (IV - into a vein) at high doses, where it can kill rapidly dividing cancer cells of many types, including leukemia. Cyclophosphamide has also been used at low doses to help regulate the immune system to enhance the body's immune response against cancer in solids tumors and lymphoma.

The purpose of this study is to determine if giving the immunotherapy drugs, nivolumab, intravenously (IV - into a vein infusion) once every 3 weeks and N-803 subcutaneously (SC -an under the skin injection) once every 3 weeks, with oral (taken by mouth) low dose cyclophosphamide is safe and results in disease control.

Duration of study treatment and follow-up:
While on study treatment, you will come to clinic once a week every week. Study treatment is planned for up to 4 months, but drugs may be continued for longer if felt to be of benefit and with acceptable side effect profile. A final treatment visit is done 1 month after your last dose of study drugs to ensure there are no ongoing side effects.

Nivolumab is given as an IV infusion every 3 weeks. N-803 is given by SC injection every 3 weeks. Cyclophosphamide is taken either once a day or once a week by mouth. A check of your blood counts will be done every week.

Follow-up for disease response and survival continues until up to 2 years from the 1st dose of study drug. If you are not being treated by University of Minnesota physicians, this follow-up information is obtained by reviewing your medical record or contacting your local doctor.
More detailed information about the study procedures can be found under "**Detailed Information About This Research Study.**"

Important risks of the study treatment:

The most common side effect associated with nivolumab is tiredness. Side effects due to cyclophosphamide include nausea, vomiting, loss of appetite, stomach ache, and diarrhea.

Other less common but more serious risks of nivolumab include an allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat during or shortly after its infusion and side effects associated with activation of the immune system (immune-related) which may include diarrhea, skin rash, changes in vision, changes in liver, kidney or thyroid function as detected on routine blood tests, and an increased risk of infection. Contact your study doctor or a member of the research staff (information on page 1) if you experience any changes in your health, even if you are not sure if it is related to the treatment.

N-803 usually causes a localized skin rash that may be large and last for a week or more. This may be uncomfortable, itchy and even painful. N-803 also may cause flu-like symptoms (fever, chills, and nausea).

You will be given medications before, during and after treatment to prevent or lessen expected side effects.

More detailed information about the risks of this study can be found under "**Risks of Study Participation."**

Potential benefits of taking part in this research study:

There may be no benefits to you from your taking part in this research. Your disease may not get better or may even get worse while you are in this study. Information from this study may help researchers in the development of future treatments for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS).

More information about the potential benefits of this study can be found under "**Benefits of Study Participation."**

Alternatives to being in this research study:

You do not have to be in this study. Alternatives may include:

- Treatment with standard chemotherapy without being in a research study
- Other investigational treatments at this institution or at another research center

- Comfort care only, where treatment is directed only at reducing symptoms, relieving suffering, and maximizing comfort, dignity, and control. In comfort care only, treatment is not directed at curing, slowing, or reversing your disease.

Your doctors can tell you more about your condition and the possible risks and benefits of the different available options.

Detailed Information About This Research Study

The following is more detailed information about this research study.

Up to 20 persons with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) will be enrolled in this study.

The 20 patients enrolled in the study are randomly assigned (like a flip of a coin) to either:

- cyclophosphamide once a day or
- cyclophosphamide once a week The total weekly dose is the same.

All patients receive nivolumab once every 3 weeks as an intravenous (into a vein) infusion, and N-803 once every 3 weeks as an SC injection.

You will be told whether you are receiving daily or weekly cyclophosphamide. Except for the cyclophosphamide dosing plan, everything in the study is identical.

Consent and study eligibility screening:

Before you can start the study, the study doctor or study staff will talk to you about the study. If you are interested in possibly taking part in the study, you will be asked to sign this consent form. By giving your consent, the necessary assessments can be done to see if you meet the requirements to receive treatment in this study. This screening period can last up to 2 weeks.

You will have the following tests or procedures (called “screening tests”) to find out if you can be in the study. These tests and procedures are part of your regular cancer care and may be done even if you do not join the study. If you have had some of these tests or procedures recently, they may not need to be repeated. This will be up to your study doctor.

- Medical history and physical examination, including vital signs, height and weight.

- Routine blood tests (requiring approximately 1 tablespoon of blood for a complete blood count (including white blood cell count, hemoglobin, platelets) and to evaluate kidney, liver, thyroid function.
- Pregnancy test – A urine or blood test for female patients who are able to become pregnant. Pregnant women are not permitted in this study.
- Bone marrow biopsy and aspiration to assess the status of your disease - often a bone marrow biopsy is done before a decision about treatment is made. You may have signed a separate consent to use the biopsy results for this study, and if so, the biopsy would not be repeated.
- Any additional tests or evaluations, felt necessary by the medical staff, to evaluate your current health.

In addition, the following will be done for research related testing:

- An additional 4 teaspoons of blood is collected for research related testing at the time you are having blood collected for your medical care.
- An additional 5 teaspoons of bone marrow cells are collected for research related testing at the time you are having bone marrow biopsy for your medical care - You may have signed a separate consent and if so, this sample would have been collected at the time of the bone marrow biopsy.

If you are not eligible for this study or decide you do not want to take part in this study, the samples collected for research purposes will be destroyed.

What will happen during this study:

If you are eligible and agree to participate and you are among the first group of patients enrolled into the study you will be randomly (like a flip of a coin) assigned to one of the two following treatment plans:

- Low dose cyclophosphamide taken by mouth once a day every day while you are on study treatment, nivolumab as an intravenous (IV – into a vein) infusion, and N803 SC injection in the clinic every 3 weeks.
- Low dose cyclophosphamide taken by mouth once a week (using the same total weekly dose) while you are study treatment, nivolumab as an intravenous (IV – into a vein) infusion, and N-803 SC injection in the clinic every 3 weeks.

Randomization is done by computer and you have an equal chance of receiving either treatment plan. Neither you nor your doctor can choose whether you receive daily or weekly cyclophosphamide.

Cyclophosphamide is taken either once a day or once week at approximately the same time of the day. The tablets must be swallowed whole, with a full glass of water. Cyclophosphamide tablets are best taken early in the day about an hour before a meal. However, to avoid queasiness, it may be taken with food and anti-nausea medication if needed. You should drink plenty of liquids while taking cyclophosphamide to lessen side effects.

Nivolumab is given once every 3 weeks in the outpatient clinic as an intravenous (IV – into a vein) infusion. The infusion is given over approximately 30 minutes.

N-803 is given in the outpatient clinic. You will be required to stay for 2 hours after the 1st injection to be sure there are no unacceptable side effects. If the 1st injection goes well, the stay time may be reduced to 30 minutes.

Each 3-week period is known as a "cycle". A treatment cycle consists of 21 days (3 weeks) with the start of a treatment cycle considered Day 1. Nivolumab and N-803 are given on Day 1. Study treatment is planned for up to 5 cycles, or about 4 months, but the study drugs may be continued for longer if felt to be of benefit and with acceptable side effect profile.

A bone marrow biopsy will be done before the start of Cycle 2 and Cycle 3 to determine your disease response and to decide if treatment should continue.

Study visits during each cycle:
Below is an outline of what is to occur at each visit; however this may be altered based on individual needs:

Before the start of each treatment cycle (on or a couple of days before Day 1):

- Brief physical assessment including vital signs and weight
- Review of symptoms, side-effects and any changes in any medications
- Blood tests (about 2 teaspoons of blood) for the evaluation of your general health
- Review of side effects and cyclophosphamide drug diary/tablet count
- A urine pregnancy test for women of childbearing potential
- Nivolumab is given
- N-803 is given

Once a week during the reminder of the treatment cycle (Day 8 and 15):

- Brief physical assessment including vital signs
- Review of side-effects
- Blood tests (about 1 teaspoon of blood) for the evaluation of your general health

Before the start of the 2nd and 3rd treatment cycles

- Bone marrow biopsy and aspirate to assess your disease response

End of treatment visit (Approximately 4 weeks after your last treatment):

- Brief physical assessment including vital signs
- Review of side effects and cyclophosphamide drug diary/tablet count
- Blood tests (about 2 teaspoons of blood) for the evaluation of your general health

The status of your disease will be followed for 2 years from the start of study treatment. This will be done by reviewing your medical record or contacting your local doctor if you are receiving care outside of University.

Research Related Sample Collection:

As this is a clinical research study, research related testing is done on blood collected during screening, weekly through the first two cycles, and every 3 weeks for cycles 3, 4, and 5. Research related testing is done on bone marrow cells collected during screening, before cycles 2, 3, and 5 (routine medical care bone marrow biopsy). Each blood sample is approximately 3 tablespoons. Each bone marrow research sample is approximately 5 teaspoons.

At the time of study enrollment you are assigned a unique participant code that will be used instead of your name or other identifying information. The research samples are labelled with your unique code making it difficult for anyone looking at the sample to know it belongs to you.

None of the research related testing results will affect your care or your participation in this study. Neither you nor your health insurance provider will be charged for the cost of research sample processing, storage and testing. No results will be placed in your medical record.

At the end of the consent form you will be asked to consent (agree to) the storage of any remaining research samples after the testing done directly related to this study is completed.

Alternatives to being in this research study:

You do not have to be in this study. The study doctor will talk to you about other treatment options, including the risks and benefits.

Your participation in this study is voluntary. You can decide not to be in the study and you can change your mind about being in the study at any time. There will be no penalty to you, and you will not lose any benefits except for benefits having to do with the study.

Your regular medical care at this study center will not change if you decide not to be in the study. Some other things you may be able to do include:

- standard chemotherapy
- other investigational treatments at this institution or at other research centers
- no treatment at this time with comfort care for your symptoms

Your doctors can provide you with additional information regarding your options.

Leaving this research:

You can leave the research at any time. Leaving will not be held against you.

If you decide to leave the research study, contact the investigator or study staff. A member of the study team may ask you some questions about being in the study. If you decide to leave the study let your study doctor know so you can receive the proper supportive care or other needed treatments.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means your decision will not negatively affect your right to any present or future medical treatment.

If you stop being in the research study, already collected information about you will not be removed from the study database. You will be asked whether the investigator can collect information from your routine medical care, such as your medical records. If you agree, this information will be handled confidentially, the same as the information obtained for the research study.

Risks of being in this study:

While receiving nivolumab, N-803 and cyclophosphamide, you may experience side effects. You may experience all, some, or none of these side effects and the side effects

may vary in severity. The severity may be mild, moderate or severe, up to and including death. Also, there is always the risk of a rare or previously unknown side effect occurring.

Other drugs will be given to make side effects less serious and uncomfortable or your doctor may decrease or withhold the dose of one or more of the drugs. Many side effects go away shortly after the study drugs are stopped, but in some cases side effects can be serious, long-lasting or permanent, even fatal.

Understanding the risks of using nivolumab and N-803 in combination with cyclophosphamide is one of the study's questions; however the risks of each drug individually is known as they have used in other cancers.

Risks of Nivolumab

Risks and side effects related to the nivolumab are mentioned below. These are not all the possible side effects associated with the drug. Nivolumab is approved by FDA for use treatment of some types of cancer including lung cancer, skin cancer (melanoma), kidney cancer, head and neck cancer, bladder cancer, and Hodgkin lymphoma. More information can be supplied by your doctor.

Severe infusion reactions. Tell your doctor or nurse right away if you get these symptoms during an infusion nivolumab:

- chills or shaking
- itching or rash
- flushing
- difficulty breathing
- dizziness
- fever
- feeling like passing out

COMMON, SOME MAY BE SERIOUS In 100 people receiving nivolumab, more than 20 and up to 100 may have:
Tiredness
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving nivolumab, from 4 to 20 may have:
anemia (low hemoglobin) which may require blood transfusion

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving nivolumab, from 4 to 20 may have:

- swelling and redness of the eye which may cause blurred vision with a chance of blindness
- pain
- diarrhea, nausea, vomiting
- colitis (abdominal pain)
- dry mouth
- fever
- headache
- cough
- upper respiratory tract infection, including pneumonia
- low or high thyroid hormone levels (hypothyroidism or hyperthyroidism)
- decreased weight
- dizziness
- swelling and redness at the site of the medication injection
- bruising, bleeding
- loss of appetite
- fluid overload in the body, including swelling in the arms or legs
- swelling of the body which may cause shortness of breath or headache, tiredness, and nerve pain
- itching, rash, skin changes

RARE, AND SERIOUS
In 100 people receiving nivolumab, 3 or fewer may have:

- damage to organs which may cause weakness or shortness of breath and/or cough visual disturbances
- swelling and pain around the eyes which may lead to vision changes and difficulty closing eyes
- a tear or hole in the stomach that may require surgery
- allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- reaction during or following a drug infusion which may cause fever, chills, rash
- a condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma muscle pain and/or weakness with dark red urine
- confusion
- abnormal movement of the facial muscles

RARE, AND SERIOUS In 100 people receiving nivolumab, 3 or fewer may have:
• weakness and paralysis • muscle weakness • numbness, tingling or pain of the arms and legs • kidney damage which may require dialysis • ventricular arrhythmia (abnormal or fast heartbeats) • type 1 diabetes

Nivolumab is an immunotherapy that works by turning on the immune system to attack the cancer cells. Nivolumab can cause your immune system to attack normal organs and tissues in many areas of your body and can affect how they work. These problems can sometimes become serious or life-threatening, and even result in death. These problems can happen at any time, even after treatment has stopped.

Contact your study doctor or study staff right away if any of these unlikely but serious side effects occur:

- lung problems (pneumonitis): new or worsening cough, chest pain, shortness of breath
- intestinal problems (colitis): diarrhea, light colored stools, blood in stools, or dark, tarry or sticky stools, stomach pain or upset stomach
- nausea (interferes with ability to eat and unrelieved with prescribed medication), vomiting (vomiting more than 4-5 times in a 24 hour period)
- unable to eat or drink for 24 hours or have signs of dehydration: tiredness, thirst, dry mouth, dark and decrease amount of urine, or dizziness
- sudden change in eyesight
- sudden onset of shortness of breath, accompanied by cough and/or fever
- skin or the whites of your eyes turn yellow
- urine turns dark or brown (tea color) or blood in urine
- big weight gain
- unable to pass urine or change in the amount of urine passed
- bleed or bruise more easily than normal
- fast heartbeat
- cough with or without mucus
- any skin change, irritation, itching or rash
- very bad muscle pain or weakness
- very bad joint pain
- swelling in the arms or legs

- signs of trouble with your thyroid or pituitary gland (change in mood or the way you act, change in weight, constipation, dizziness, deeper voice, feeling cold, fainting, hair loss, feeling very tired, headache or loss of sex drive)

You may experience one or more of the risks listed below with N-803. In addition to these, there may be other unknown risks, or risks that are not anticipated in association with the drug. Some risks described in this consent document, if severe, may cause death.

The most common side effects seen in studies with subcutaneous (under the skin) injections have been fever, fatigue, chills, and an injection site reaction with an associated skin rash, which at times has been widespread. These localized skin reactions are common (occurring in more than 50% of patients). You will receive medications to reduce the risk and/or severity of expected side effect. The skin rash may be treated with steroid cream if it causes discomfort.

Risks of N-803 when given as a subcutaneous injection		
Very common (more than 1 in 10 patients experience)	Common (between 1 in 30 and 1 in 10 patients experience)	Rare (fewer than 1 in 30 patients experience)
• injection site reaction (skin rash), which may be large (> 2 inches), itchy, and/or painful • fever • chills which maybe "shaking" • feeling tired or short of breath due to a low red blood count (anemia) which could cause you to faint • changes in blood pressure – low blood pressure may cause lightheadedness • nausea • swelling of hands or feet • temporary changes in routine lab results including decreased albumin and	• flu-like symptoms, including headache, muscle, or joint pain • fatigue • decreased appetite • diarrhea, vomiting • abdominal pain • itchy skin and/or skin irritation • shortness of breath • high blood sugar (hyperglycemia) • changes in electrolytes on routine lab work	• inflammatory reaction (pain, localized warmth, redness, and swelling) of the injection site • infection including upper respiratory infection • atrial fibrillation (a-fib) – you may not have symptoms, but when symptoms do appear they may include irregular and often rapid heartbeat, shortness of breath, and fatigue

Risks of N-803 when given as a subcutaneous injection		
Very common (more than 1 in 10 patients experience)	Common (between 1 in 30 and 1 in 10 patients experience)	Rare (fewer than 1 in 30 patients experience)
decreased lymphocytes		

Tuberculosis is a potential risk of N-803. One instance of tuberculosis has been reported in a participant receiving N-803 in combination with BCG (a live, attenuated strain of Mycobacterium bovis) administered into the bladder by a urinary catheter. A causal relationship between N-803, in combination with BCG, and tuberculosis infection cannot be definitely ruled out.

Anti N-803 antibodies have been detected in subjects receiving N-803. The impact of antiN-803 antibody formation on clinical efficacy and safety of N-803 is unknown.

Risks of the Combination of Nivolumab and N-803

The combination of N-803 + nivolumab has been associated with injection site reaction, flu-like symptoms, fever, fatigue, nausea, pain, chills, dizziness, low blood pressure, cough, shortness of breath, loss of appetite, constipation, and vomiting.

Possible increase in risk of graft-versus-host disease (GVHD) due to N-803: GVHD is an expected complication of transplants using donor cells from another person. GVHD occurs when the donor cells (the graft) see the patient cells (host) as foreign and attack them. Even though you have not had a transplant, you may still be at risk for GVHD-like symptoms by taking N-803. A skin rash, diarrhea, and/or a change in blood liver function tests are possible signs of GVHD.

While on N-803, you will have a brief assessment before each injection looking, in part, for signs of GVHD. A skin rash outside of the injection area is one sign. If you do develop GVHD or it is suspected, the remainder of the N-803 doses for the current cycle will be held and you will be started on standard GVHD treatment. In some cases, a biopsy will be done to confirm GVHD. N-803 may be restarted with the next planned cycle if the GVHD has improved with standard treatments. In cases of severe GVHD, N-803 would be permanently stopped.

Risks of Low-Dose Cyclophosphamide

Nausea, vomiting, loss of appetite, stomach ache, diarrhea, or darkening of the skin/nails may occur. Nausea and vomiting can be severe. In some cases, drug therapy may be necessary to prevent or relieve nausea and vomiting. Changes in diet such as eating

several small meals or limiting activity may help lessen some of these effects. If these effects persist or worsen, notify your doctor or study staff promptly.
Tell your study doctor or study staff right away if any of these unlikely but serious side effects occur:

- signs of kidney or bladder problems (such as change in the amount of urine, pink/bloody urine)
- mouth sores
- unusual tiredness or weakness
- joint pain
- easy bruising/bleeding
- stopping of menstrual periods
- existing wounds that are slow healing
- black/bloody stools
- severe stomach/abdominal pain
- yellowing eyes or skin
- dark urine
- mental/mood changes
- muscle weakness/spasm
- swelling of the ankles/feet
- sudden or unusual weight gain

This medication can lower the body's ability to fight an infection. Notify your doctor promptly if you develop any signs of an infection such as fever, chills or persistent sore throat.

These are not all the possible side effects associated with cyclophosphamide. More information can be supplied by your doctor.

Risk to unborn children:

If you or your partner is considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant.

<u>For Women:</u>
If you are pregnant, you cannot participate in this study, because there may be risks to you and your unborn baby that are currently unforeseeable (risks that we do not know

about yet). Breastfeeding (nursing) mothers will not be included in this study since it is not known whether the drugs in this study will be passed on to the baby in mother's milk. If you are currently breastfeeding and wish to continue breastfeeding, your study doctor may recommend another treatment.

If you are a female of childbearing potential (able to become pregnant), you will be given a pregnancy test before beginning each cycle of drug (every 4 weeks).

For Men:

It is not known what nivolumab could do to your sperm. Should you get a woman pregnant, there could be harm to the unborn baby. You and your partner should use an effective form of birth control if your partner is a woman of childbearing potential.

For Men And Women:

Whether you are a man or a woman, there may be risks to your unborn children that we don't know about ahead of time; they are unforeseeable. If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. Females must not get pregnant or breastfeed for 23 weeks after the last dose of nivolumab and N-803. Males should continue birth control with women of childbearing potential for 31 weeks after the last dose of nivolumab and N-803.

According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable but less effective methods of birth control include male condoms (with or without spermicide) and female condoms.

Whether you are a woman or a man, you should tell your study doctor immediately if you become pregnant or if your partner becomes pregnant. Women who become pregnant during the study will have to leave the study treatment. The study doctor or study staff will ask for information about the pregnancy and the birth of the baby. The study doctor or study staff may share this information with the University of Minnesota IRB (a group of people who review research studies to protect the rights and welfare of research participants) and Bristol-Myers Squibb (BMS – the manufacturer of nivolumab).

Cancer treatment can affect fertility in both men and women, and it is important to understand the risks before starting therapy. Ask your staff about fertility preservation before you begin treatment. However, once you have started treatment you should not donate or sell your eggs or sperm.

Risks of Blood Collection:

Risks of having blood drawn for routine blood tests and research purposes include:

- pain at the site of the needle stick
- tenderness and/or bruising at the site of blood collection
- dizziness or light-headedness
- very rarely, infection at the site of the needle stick

Risks of Bone Marrow Biopsy and Aspiration:

You will sign a separate surgical consent form before the biopsy is done. A biopsy is generally a safe procedure. Serious problems are rare. Possible risks can include:

- Pain at the biopsy site is the most common complication after a biopsy.
- A small amount of bleeding from the biopsy site can be expected

Complications are rare but can include:

- Excessive bleeding, particularly in people with low numbers of a certain type of blood cell (platelets).
- Infection, especially in people with weakened immune systems. Long-lasting bruising or discomfort at the biopsy site.

The risks of **collecting extra bone marrow cells** for research purposes at the time a bone marrow biopsy is done for your medical care does not increase the risk of this procedure.

Benefits Of Taking Part In This Research:

There may be no benefits to you from your taking part in this research. Your disease may not get better or may even get worse while you are in this study. We cannot promise any benefits to others from your taking part in this research. Information from this study might help researchers to come up with new tests or medications to help others in the future. However, possible benefits to others include development of future treatments for acute myeloid leukemia or myelodysplastic syndrome.

Research Related Injury:

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such

injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research related injury, let the study physicians know right away.

Duration of Study Participation:
Up to 5 treatment cycles of nivolumab, N-803, and cyclophosphamide are planned; however, one or all drugs may be discontinued earlier if any of the following occurs:

- your disease worsens
- you experience unacceptable side effects
- a delay of more than 4 weeks occurs from a planned treatment cycle start
- you are unable to comply with the study requirements
- if the study doctor believes, for any reason, continuing on treatment is not in your best interest
- if the study is stopped early

Disease and survival status obtained from your medical record or other sources will be collected for up to 2 years from any patient receiving at least one treatment cycle.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

Costs:
Nivolumab and oral cyclophosphamide will be provided free of cost by its manufacturer Bristol-Myers Squibb. N-803 will be provided free of cost by NantCell Inc. Research (ImmunityBio) related testing on blood and bone marrow cells will be paid for by research funds. Thyroid function tests, although routine will be paid for by the study.

You and/or your insurance company will be responsible for the remaining costs related to this treatment including but not limited to the clinic visits, routine lab work, scans or imaging for disease assessment, any medications given to prevent or treat side effects, and expenses associated with bone marrow biopsy procedures. You will be responsible for any costs your insurance does not cover, such as deductibles and co-payments. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

You will not be paid for taking part in this study.

Confidentiality and Privacy:

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information including those that have responsibilities for monitoring or ensuring compliance include:

- Research personnel from the Masonic Cancer Center and/or their designee
- The Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution.
- Any federal, state, or local governmental agency that regulates the study such as the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP).
- NantCell (ImmunityBio) and/or their designee.

Bristol-Myers Squibb, the maker of nivolumab, will receive reports of serious adverse events with indirect identifiers (using the code assigned to you at study enrollment).

The Masonic Cancer Center, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access.

The results of this study will be used for teaching, publications, or for presentation at scientific meetings. The results also may be summarized in the background section of future research studies and publications. Results will never include information to allow an individual patient to be identified.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. The web site will include a summary of the results after the study is completed. You may search this web site at any time.

Use of Identifiable Health Information

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Contacts and Questions:

Information for contacting the study's Lead Physicians and Study Coordinator is provided on the 1st page of this document.

This research has been reviewed and approved by an Institutional Review Board (IRB) within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 or go to www.irb.umn.edu/report.html. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Feedback:

After the study, you may be asked to complete a survey about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey after the study is over, but you would like to share feedback, please contact the study team or the Human Research Protection Program (HRPP). See the "Contacts and Questions" section of this form HRPP contact information.

CONSENT FOR OPTIONAL STORING OF LEFTOVER RESEARCH SAMPLES

There may be some leftover blood and/or bone marrow cells from the samples collected for research purposes. With your permission; we would like to store them for up to 15 years after the study ends for future analysis as new research tests become available. These samples will be the property of and under the control of the Principal Investigator Joseph Maakaron, MD. They will not be used for studies other than ones to learn about the blood cancers and/or the immune system.

The samples will be stored with indirect identifiers. They will be labeled with a unique code number, rather than a name or medical record number, and the samples can only be linked back to the patient using a master list for the study. This master list will be kept in a secured manner and only accessible to persons directly involved with the research.

There will be no cost to you for storing and future testing of the leftover samples. You will not be paid for allowing your samples to be used for future research. Because it is not known how soon these samples will be used, you will not be given the results of the tests.

Fifteen years after the end of the study any remaining samples will be destroyed. However, if you agree to storage now and later change your mind, you may request to have any remaining identifiable samples destroyed by contacting the study doctor or another member of the study staff.

Consent for Storage of Leftover Samples for Future Research

☐ YES, I consent (agree) to the storing of any leftover samples for future research

☐ NO, I do not consent (do not agree) and want any leftover samples destroyed once research directly related to this study is completed.

STATEMENT OF CONSENT

I have read the above information. I have asked questions and have received answers. I agree to take part in this research study.

_____

Subject's Printed Name

_____ _____

Subject's Signature Date

I have explained fully the above objective of this study, what is to be expected and the possible complications.

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Principal Investigator or Delegate Obtaining Consent Date

WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is unable to read the information

☐ The participant is visually impaired

☐ The participant is non-English speaking

☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:
A**s** someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Interpreter Date

_____ Printed

Name of Interpreter

Statement from a Non-Interpreter:

As someone who understands the language spoken by the subject (English or otherwise), I represent that the version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Individual Date

_____

Printed Name of Individual