

MC1562 / 15-007000

Phase I Trial Of Intravenous Administration Of Vesicular
Stomatitis Virus Genetically Engineered To Express Thyroidal
Sodium Iodide Symporter (NIS) And Human Interferon Beta
(HIFNb) In Patients With Metastatic Or Recurrent Endometrial
Cancer

NCT03120624

Document Date: 10/18/2023



Approval Date: October 18, 2023
Not to be used after: February 17, 2024

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1562 Phase I Trial of Intravenous Administration of Vesicular Stomatitis Virus Genetically Engineered to Express Thyroidal Sodium Iodide Symporter (NIS) and Human Interferon beta (hIFN β), in Patients with Metastatic or Recurrent Endometrial Cancer (Group B)

IRB#: 15-007000

Principal Investigator: Dr. J. Bakkum-Gamez and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.

It's Your Choice

This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.

Research Purpose

The purpose of this research is to find out whether a viral agent called Vesicular Stomatitis Virus can help patients with metastatic endometrial cancer.

The study virus used in this study is considered investigational, which means it has either not been approved by the Food and Drug Administration (FDA) for routine clinical use or for the use described in this study. However, the FDA has allowed the use of this virus in this research study.

You have been asked to take part in this research because you have been diagnosed with either Stage IV endometrial cancer or your cancer has not responded to standard treatments and has come back.



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What's Involved	Study participation involves the following (which are part of regular care for your cancer): • Medical history and physical exam including vital signs • Imaging of your tumors • Routine blood tests The study also requires the following procedures which are done only for research: • Administration of ruxolitinib starting 3 days prior to virus administration • Tests of immune function • Blood levels, urine and mouth swabs to check levels of VSV-hIFNβ-NIS • The virus and its administration (VSV-hIFNβ-NIS) • Optional NIS imaging scans to see where the virus goes in your body – if available • Additional biopsies just for research • Your stay at the hospital to receive the VSV-hIFNβ-NIS
Key Information	This research study is a phase I clinical trial in which the research team is studying the safety of a virus (VSV-hIFNβ-NIS) in women with endometrial cancer that has spread or recurred. Because this is a new treatment being studied in humans, some risks of the virus are not yet known. The most important risks include the potential side effects of the virus. These most often include a temporary fever and chills a few hours after receiving the virus and temporary blood count and liver enzyme changes within a few days after receiving the virus. You will be hospitalized while you receive the virus and for 24-48 hours after the virus is given to observe you for early side effects. There is a risk of needing another hospitalization for virus side effects and you will be watched closely with blood draws, checks for symptoms that may be related to the virus and physical exams after receiving the virus. This will require you to stay near Mayo Clinic for close monitoring during the week or two after receiving the virus. The further out you are from receiving the virus, the less frequent these blood draws, symptom checks, and physical exams will be. There is also a risk that the virus could cause a life-threatening infection or destruction of cancer rapidly enough to be life-



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	threatening. Your research team feels this risk is low and has treatment plans in place if a life-threatening situation were to arise. The other risks, discomforts and/or inconveniences of this study include those associated with blood draws, urine collection, mouth rinse, and mouth swab collection; NIS imaging, which requires an IV and receiving an imaging dye; and tumor biopsies. Other treatment options for your cancer may include chemotherapy regimens, radiation, surgery, or another clinical trial. Options for your cancer are determined based on where the cancer has spread to in your body and the number of places it has spread to. Your healthcare provider will tell you what options are suitable for your cancer treatment.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.



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Contact Information

If you have questions about ...	You can contact ...
• Study tests and procedures • Materials you receive • Research-related appointments • Research-related concern or complaint • Research-related injuries or emergencies • Withdrawing from the research study	Principal Investigator: Dr. Jamie Bakkum-Gamez Phone: (507) 284-2511 Institution Name and Address: Mayo Clinic 200 First St SW Rochester, MN 55905
• Rights of a research participant	Mayo Clinic Institutional Review Board (IRB) Phone: (507) 266-4000 Toll-Free: (866) 273-4681
• Rights of a research participant • Any research-related concern or complaint • Use of your Protected Health Information • Privacy concerns related to data collected in the European Economic Area. • Stopping your authorization to use your Protected Health Information • Withdrawing from the research study	Research Participant Advocate (RPA) (The RPA is independent of the Study Team) Phone: (507) 266-9372 Toll-Free: (866) 273-4681 E-mail: researchparticipantadvocate@mayo.edu
• Billing or insurance related to this research study	Patient Account Services Toll-Free: (844) 217-9591

Other Information:

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.



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Why are you being asked to take part in this research study?

You are being asked to be in this study because you have been diagnosed with either Stage IV endometrial cancer or your cancer has not responded to standard treatments and has come back.

Since your tumor burden is greater than other patients with your disease, you will be receiving an additional drug (ruxolitinib) to help control the side effects of treatment.

Why is this research study being done?

The primary purpose of this study is to find out whether a viral agent called Vesicular Stomatitis Virus can help patients with metastatic endometrial cancer. The study virus has a gene inserted into it which will allow for the production of interferon beta, which is a substance that will have the dual functions of restricting the spread of the virus to the tumor cells and not healthy cells and also to have some independent anti-cancer activity.

The virus has been altered by having an extra gene (piece of DNA) added for a protein called NIS inserted into it. NIS is normally found in the thyroid gland (a small gland in your neck) and helps the body concentrate iodine. Having this additional gene will make it possible to track where the virus goes in your body.

The study virus used in this study is considered investigational, which means it has either not been approved by the Food and Drug Administration (FDA) for routine clinical use or for the use described in this study. However, the FDA has allowed the use of this virus in this research study.

This virus has been tested in humans before, and it is not a vaccine. This study is being done to:

- Test the safety of the intravenous administration of VSV-hIFN β -NIS.
- Test whether the VSV-hIFN β -NIS makes patients' cancer better.
- Determine the fate of the virus (where it is, how long it stays there, how it multiplies) in the body using NIS imaging by either SPECT/CT or TFB-PET. These scans use small doses of radioactive isotope (m99Tc or 18F-tetrafluoroborate [TFB]) routinely to image the thyroid and other organs without any known problems.
- Evaluate the effects of the virus on the body using blood, throat swabs, urine samples and biopsies



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Information you should know

Who is Funding the Study?

The National Cancer Institute (NCI) and the David F and Margaret T Grohne Foundation are funding the study. They will pay the institution to cover costs related to running the study. Some of the costs will be covered by benefactor donations made to Mayo Clinic to support this study.

Information Regarding Conflict of Interest:

This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and is being conducted in compliance with Mayo Clinic Conflict of Interest policies.

Both the Mayo Clinic Conflict of Interest Review Board and the Institutional Review Board have reviewed the Financial Conflict of Interest for one or more of the investigators and/or Mayo Clinic related to this research, and they have determined that this Financial Conflict of Interest poses no additional significant risk to the welfare of participants in this research project or to the integrity of the research.

Additional information is available to any interested study participant regarding the details of this Financial Conflict of Interest and how it is being managed by contacting the study coordinator or the Office of Conflict of Interest Review at (507) 284-0075.

One or more of the investigators associated with this project and Mayo Clinic have a Financial Conflict of Interest in technology used in the research and that the investigator(s) and Mayo Clinic may stand to gain financially from the successful outcome of the research.

How long will you be in this research study?

You will be in the study for up to 1 year after you receive the VSV-hIFN β -NIS or until your cancer gets worse. We will continue to monitor your health for up to five years.

The plan is to have up to 77 people take part in this study.



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What will happen to you while you are in this research study?

If you agree to be in the study, you will be asked to participate in the following:

Screening Visit

Prior to starting treatment on this trial, you will have specific procedures and tests to make sure you are eligible to be in this study. They include:

- Medical history (including any medications that you are taking now or have taken in the past)
- Review of your current medical condition(s)
- Physical examination (including weight)
- Vital signs (blood pressure, heart rate, temperature, breathing rate, etc.)
- Electrocardiogram (ECG) to see how your heart is working
- CT scan of your chest, abdomen and pelvis
- Routine blood tests
- Biopsy of your cancer

These tests are part of regular care for your cancer. If some of these tests have been done recently, you may not need to repeat them.

In addition, the following tests will need to be done for participation in this research study.

- HIV, hepatitis, and tuberculosis testing
- Pregnancy test if you are able to become pregnant
- Optional baseline NIS imaging scan by TFB-PET if available – these scans are used to determine the fate of the virus (where it is, how long it stays there, how it multiplies) in the body using. These scans use small doses of radioactive isotopes (18F-tetrafluoroborate [TFB]) routinely to image the thyroid and other organs without any known problems.

These are research tests and you will not have to pay for them.

If it is not known whether you have HIV, you will need to have a blood test done. If your HIV test result is positive you will need to have a second test done to make sure the results are the same. If you are infected with HIV, the researcher will tell you how to find medical help and counseling as needed, and you will not be able to take part in the study. Your health insurer or you will have to pay for the cost of the repeat test, any follow-up medical care, or counseling. If the HIV test results are positive, it is state law that they be reported to the State Department of Health. The test results will also be put in your medical record.



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Prior to virus administration visit

Because the burden of your cancer is greater than other patients with your disease, you will be given ruxolitinib to help manage the side effects of your treatment. Ruxolitinib will be provided to you as a pill, and you will need to take it twice a day starting three days prior to your virus administration visit and ending 9 days after your treatment with VSV- hIFN β -NIS (for a total of 12 days).

Virus administration visit

If you are eligible and choose to take part in the study you will have the following:

You will be admitted to Mayo Clinic Hospital – Methodist Campus the day before VSV-hIFN β -NIS virus infusion.

Research blood samples, mouth rinse, cheek swab, and urine samples will be taken before the virus infusion.

The VSV-hIFN β -NIS will be given slowly by vein while you are monitored closely for potential side effects until the next day.

Research blood samples will be collected right after completing the intravenous VSV-hIFN β -NIS, 30 minutes after infusion, 1 hour after infusion, 2 hours after infusion, 4 hours after infusion, and 20-24 hours after infusion. Mouth rinse and urine samples will be taken 20-24 hours after the infusion.

As long as you are doing fine, you will be allowed to leave the hospital about 48 hours after the virus infusion (Day 2-3). We ask that you stay within 30 miles of Rochester, Minnesota, for 10-15 days until your study doctor thinks it is safe for you to go home.

After you leave the hospital, you will need to come back to the clinic every day for the next three (3) days (Days 3-5) for a quick check of your vital signs (temperature, heart rate, pulse, and respiration rate) and clinical blood testing to see how your body is handling the virus.

These checks are very important for your safety. You must tell the study team of any new symptoms each time.

We will also take some research blood and urine samples on Day 3 to look at virus levels.

If available, you may have another NIS imaging scan about 2 days after VSV-hIFN β -NIS injection; you will be given radioactive isotope (tetrafluoroborate [TFB]) by vein before the scan. NIS imaging scans with TFB-PET involve exposure to x-rays. These studies will take place at the Department of Nuclear Medicine at Mayo Clinic.



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If the virus is still showing in your body, this scan may be repeated on Day 10; (give or take a day or two) after taking another dose of radioactive isotope. An additional NIS imaging scan may also be repeated between Day 2 and Day 10 or after Day 10 if your doctor or the study team thinks another scan is needed.

If there is an area that “lights up” on one of the NIS imaging scans, suggesting that there may be virus at that location, and if it is in a position in your body that is easy to biopsy, you may have a small needle to be inserted into that area to obtain tissue for research purposes (a biopsy). This biopsy will be covered by the study and is free of charge to you.

If my NIS imaging scan shows possible active virus, I agree to have a research biopsy done.

☐ Yes ☐ No Please initial here: _____ Date: _____

Research blood, urine, and mouth swab and mouth rinse samples will be collected from you before starting treatment and on Days 3, 8, 10 and 15. If there is persistent virus, additional samples will be collected on Day 29.

Since other patients on the Mayo Clinic grounds may be severely immunosuppressed, we will require that you wear a mask when you are outside of your hospital room on Mayo Clinic grounds. The results of these tests will determine how long you should wear a mask when in public.

A biopsy of your cancer will be performed approximately one month and 3 months after administration of the virus to check on the status of the VSV-HIFNB-NIS and the endometrial cancer.

Schedule for patients receiving VSV-hIFN β -NIS

Timing	What will happen
Pre-Study	• Physical exam including medical history, height, weight, vital signs (blood pressure, pulse, temperatures, etc.), and performance status • Routine blood and urine tests and exams • Routine CT scan of chest, abdomen, and pelvis • Blood tests for HIV, hepatitis and tuberculosis • Electrocardiogram (ECG)
On-Study prior to virus administration	• OPTIONAL: Baseline NIS imaging with TFB-PET scan – if available • Check into Mayo Clinic Hospital Methodist Campus • Pregnancy test if you are able to become pregnant • Research mouth rinse, cheek swab, blood and urine collection



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Timing	What will happen
Virus administration Day 1 and Day 2	• Begin ruxolitinib three days prior to virus administration • VSV-hIFNβ-NIS infusion over 60-90 minutes • Research blood collection at 30 minutes, 1 hour, 2 hours, 4 hours after infusion • Observation in the hospital for up to 48 hours after virus administration • Research mouth rinse, cheek swab, blood, and urine collection 20-24 hours after virus infusion • Routine blood and urine tests • Continue ruxolitinib • Day 2 only: One optional NIS imaging scan (a nuclear imaging scan for research) – if available
Days 3-5 after infusion	• Assessment of any symptoms from the virus • Routine blood tests every day • Optional biopsy if any tissue still lights up with virus on imaging • Research mouth rinse, cheek swab, blood and urine collection • Physical exam on Day 5 • Continue ruxolitinib
Days 7-10 after infusion	• Assessment of any symptoms from the virus • Optional NIS imaging scan, if needed • Optional research biopsy if one was not done Days 3-5 • Routine blood tests Days 8 and 10 • Research mouth rinse, cheek swab, blood and urine collection Days 8 and 10 • Continue ruxolitinib until Day 9 NOTE: If all is well at your Day 10 visit, and your study doctor agrees, you will be allowed to go home until your next appointment on Day 15.
Day 15	• Physical exam • Optional research biopsy if one was not done previously • Assessment of any symptoms from the virus • Routine blood tests • Research mouth rinse, cheek swab, blood and urine collection
Day 29 after infusion	• Physical exam • Assessment of any symptoms from the virus • Routine CT scan of chest, abdomen, and pelvis • Tumor biopsy • Routine blood tests



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Timing	What will happen
	Research blood collection, and mouth rinse, cheek swab, and urine collection if virus still active
6 weeks after infusion	- Physical exam - Assessment of any symptoms from the virus - Routine and research blood tests
3 months after infusion	- Physical exam - Assessment of any symptoms from the virus - Routine CT scan of chest, abdomen, and pelvis - Tumor biopsy - Routine and research blood tests
6 months after infusion	- Physical exam - Assessment of any symptoms from the virus - Routine and research blood tests - Routine CT scan of chest, abdomen, and pelvis
12 months after infusion	- Physical exam - Assessment of any symptoms from the virus - Routine and research blood tests - Routine CT scan of chest, abdomen, and pelvis

You will be monitored on a regular basis for up to 5 years to check for possible long-term side-effects of the virus as well as the potential improvement of your cancer from the therapy. If your disease has progressed and you are being monitored for potential long-term side-effects, some tests may be done by your local doctor.

Special Considerations

Because we need to understand how the virus affects the cancer and your body, we are requesting two additional items as a condition of participation in this Phase I study.

- 1) We ask that you be willing to have life supportive care measures (such as dialysis) taken if you have a reaction to the virus within 30 days of administration.

Please initial here to indicate whether you understand and agree with this request:

☐ Yes

☐ No

Please initial here: _____ Date: _____



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2) In addition, should you pass away during the 12 months following virus administration; we ask that you be willing to have an autopsy.

Please initial here to indicate whether you understand and agree with this request:

☐ Yes ☐ No Please initial here: _____ Date: _____

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up, and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

Risks from the Study Virus Itself

Vesicular Stomatitis Virus Genetically Engineered to Express Thyroidal Sodium Iodide Symporter (NIS) and Human Interferon beta (hIFN β) (VSV-hIFN β -NIS) is a novel viral agent which is currently being used for the first time in humans through this trial and one other in patients with hematologic cancers. As such, many risks of the study virus in humans are unknown. However, some data regarding potential adverse effects are available. VSV-hIFN β -NIS has been tested extensively in mice, dogs, and pigs with elevation in liver enzymes being the most common side effect in dogs. However, one dog with lymphoma treated with VSV-hIFN β -NIS through the intravenous route died of tumor lysis syndrome and respiratory failure 50 hours after receiving the virus.

A similar virus strain, Vesicular Stomatitis Virus Genetically Engineered to Express Human Interferon beta (hIFN β) (VSV-hIFN β) is currently being tested as an injection directly into tumors in humans with cancer involving the liver. After 11 patients were treated without major side effects, the 12th patient experienced rapid virus replication, liver dysfunction, kidney failure, and died. This death may have been due to tumor lysis syndrome. Tumor lysis syndrome, which can cause salt imbalances in the blood and even kidney failure and is caused by the dead tumor cells in the body, can happen if the virus kills cancer cells too rapidly. Additional precautions to monitor for and aggressively treat liver dysfunction, tumor lysis syndrome, or any other life-threatening side effect if it occurs have been built into the trial you are considering. However,



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liver dysfunction, tumor lysis syndrome, and other side effects due to the virus's activity on cancer cells remain possible risks of this trial.

The trial you are considering is the first trial to use intravenous (IV) administration of the drug. It is not known whether the IV administration carries the same risks seen in the patients receiving intratumoral injection, but it is possible.

Since you are getting a viral agent, there is always the risk for a condition called "cytokine release syndrome" (CRS) in which exposure to foreign viral proteins triggers the immune system to counteract these foreign substances. The resulting effect is a syndrome characterized by fevers, chills, and shaking, and in severe cases, a drop in blood pressure, and severe allergic reaction symptoms such as swelling of the throat, skin rash and difficulty breathing. One patient on this study had a temporary delirium that lasted less than 12 hours. One patient has had weakness and tremors. Appropriate measures will be in place to handle these uncommon but severe situations. Other adverse effects at this time are unknown, and a comprehensive safety monitoring plan is in place to ensure that any adverse events that may be a threat to your safety are quickly dealt with. As with any medication, allergic reactions are a possibility (the cytokine release syndrome described above represents a severe reaction of this kind).

The wild type virus (without genetic recombination of an inserted human beta interferon gene) has been associated with a flu-like illness characterized by fever, chills, muscle aches, weakness, sore throat, headache, nausea and vomiting and occasionally lip or mouth sores. This type of syndrome has been rare, and only isolated cases have been reported in a period of observation of around a century. One case of encephalopathy (changes in neurological status) has been reported in a child with the wild type virus. The risk of this type of severe side effect is felt to be low due to insertion of the human beta interferon gene in the study agent.

Rarely, patients can develop life-threatening toxicity caused by the interferon beta in the virus itself. Symptoms of this toxicity include not recovering from the early reaction to the VSV infusion, feeling very tired with low blood pressure or low oxygen, feeling confused and signs in your lab tests that your liver is not working properly and your blood platelets are dropping. This toxicity can be fatal.

The interferon beta toxicity can also be associated with another type of toxicity called tumor lysis syndrome, where your tumor cells burst and cause problems throughout the body. This event in itself can also be life-threatening, but if diagnosed early can be treated with IV fluids and drugs.

For this reason, you will have daily blood tests and your doctor may keep you in hospital for longer than expected. If you show signs of the serious interferon beta toxicity, your ruxolitinib dose may be increased.



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Ruxolitinib (Jakafi®)

Following is the list of side effects associated with longer term use of ruxolitinib. Because you will only receive ruxolitinib for a short time (10 days) it is considered less likely that you will experience side effects related to this drug.

Likely risks of ruxolitinib (*events occurring greater than 20% of the time*)

- Low white cell count (may make you more likely to get an infection)
- Low red cell count (may make you tired and weak) and low platelet count (may make you more likely to bruise or bleed). These issues may lead to a new need or increased need for red cell and/or platelet transfusions.
- Loose stools (diarrhea)
- Feeling tired (fatigue)
- Abnormal heart sound (murmur)
- Headache
- Pain in hands and legs
- Weight increase
- Feeling sick to your stomach (nausea) or throwing up (vomiting)
- Joint pain
- Cough
- Shortness of breath or difficulty breathing (dyspnea)
- Infection of the lungs (pneumonia)
- Fever
- Hematoma or bruise
- Elevated liver function tests (AST/ALT) which may indicate that your liver is not working properly

Less likely risks of ruxolitinib (*events occurring less than or equal to 20% of the time*)

- Pain in the abdomen
- Inability to sleep or sleep disturbance (insomnia)
- Infection of the nose, sinuses and/or throat (upper respiratory infection)
- Back pain
- Muscle spasms
- Night sweats
- Intestinal gas (flatulence)
- Lightheadedness or dizziness
- Rash
- Infection in the bladder and/or kidney (urinary tract infection)
- Bronchitis



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- Difficulty passing stool (constipation)
- Shingles (herpes zoster)
- Increased uric acid in blood
- Inflammation of the nasal sinuses (sinusitis)
- Bone pain
- Feeling sad or blue (depression) and/or anxiety
- Nosebleed
- Itchiness or redness of the skin (dermatitis)
- Muscle pain
- Weakness
- Influenza (flu)
- Swelling of hands and feet (edema)
- Frequent and urgent need to urinate
- Change in heart rhythm - may feel your heart beating rapidly or feel fluttering in your chest- this effect can be serious or life threatening
- High blood levels of fat (hypercholesterolemia)

Rare but serious risks of ruxolitinib (*events occurring less than 2-3% of the time*)

- Change in blood salts that may lead to tiredness, disorientation, headache, muscle cramps, and nausea; if severe it may also lead to seizures or coma
- Cancer of lymph nodes (lymphoma) or development of other secondary malignancies may occur
- Abnormal inflammatory reaction involving the lungs (pneumonitis) and heart (pericarditis) that might be associated with shortness of breath and low blood oxygen (hypoxia)
- Bleeding from in the brain (Intracranial) or stomach, large intestine and/or small intestine (GI)
- A serious infection of the brain (progressive multifocal leukoencephalopathy)
- Heart attack

There are risks related to stopping doses of ruxolitinib which are explained below.

Serious risks that might be associated with discontinuation of treatment with ruxolitinib:

Patients with symptomatic heart or lung disease might experience serious and life-threatening deterioration of their heart or lung condition upon discontinuation of treatment with the study drug. Your doctor will decide whether or not you are eligible for the study based on your current status regarding heart or lung disease. Therefore, it is important that you disclose to your doctor history of any heart or lung disease. Other risks that might be associated with discontinuation of



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study drug include anxiety, insomnia or weakness, and recurrences of the signs and symptoms of your disease.

If the decision is made to stop ruxolitinib, your study doctor may decide to taper it based on his/her clinical judgment of your condition. Taper means to gradually lower your dose over a period of time until it is eventually stopped. If a decision is made to stop ruxolitinib without tapering, and within two weeks of stopping ruxolitinib you experience undesirable symptoms which, in your doctor's opinion, are as a result of stopping ruxolitinib, then your doctor may decide to restart the drug and taper it gradually until it can be completely stopped.

In all patients on ruxolitinib, there will be close monitoring of vital signs and other clinical parameters during drug discontinuation and the drug will be weaned slowly in the setting of an underlying cardiopulmonary condition or systemic inflammatory response syndrome. Participants on ruxolitinib should not discontinue its use unless closely monitored by the study doctor.

Despite careful laboratory testing and the close monitoring included in this study, administration of ruxolitinib may involve other risks that are currently unknown and cannot be predicted, including the possibility of serious side effects or death.

Risks of Transmission of Virus to Others

The risk of transmission of the virus to individuals other than the patient is unknown but is felt to be of very low likelihood (less than 0.1%). In the event of infection with the virus, you will need to be isolated and quarantined until it is felt by your treating physician that you have recovered from the infection and that you have a very low potential to infect others.

Radioactive 18F-tetrafluoroborate (TFB) and Radiation Risks

This isotope or a similar imaging agent may be given to you by vein to see where the VSV-hIFN β -NIS therapy has gone in your body. You may have up to four (4) doses of radioactive isotope prior to NIS imaging. You will be exposed to radiation during the radioactive isotope administrations and due to x-rays from the scanners. The amount of radiation you will receive has a low risk of harmful effects. You may receive low doses of radioactive isotope on up to 3-4 occasions for the purpose of scanning for the virus.

Risks of Biopsy

The most common problems include mild pain and a minor decrease in blood pressure. More serious complications, such as bleeding, infection, and injury to nearby organs, are very rare. If the biopsy is performed using CT guidance, you will be exposed to radiation. The amount of radiation you will be exposed to has a low risk of harmful effects.



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Risks of Blood Draw

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Birth Control and Pregnancy

The effect of VSV-hIFN β -NIS on a fetus (developing baby still in the womb), or on a breastfeeding infant is unknown and may be harmful.

You should not become pregnant while on this study. Because of these risks, patients cannot take part in this study if they are pregnant or breastfeeding.

If you are able to become pregnant, you must have a negative pregnancy test in order to participate in this study.

For the pregnancy test, you will give a blood sample taken from a vein in your arm with a needle before the study and starting the study drug. You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study.

If you are sexually active and able to become pregnant, you should discuss appropriate methods of contraception with your doctor.

If you are able to become pregnant, you must use contraception for the entire study and for at least one year after your last dose of study drug.

A pregnancy test can be wrong. If you become pregnant or think you may be pregnant during the study, contact the study doctor's office immediately. The study doctor must follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished.

You must not breast-feed/chest-feed an infant during the study. The study drug may cause unforeseeable risk to a breastfed/chest fed baby.

You must NOT be an ovum or blood donor while you are being treated with VSV-hIFN β -NIS.

Risk Summary

Many side effects go away shortly after the VSV-hIFN β -NIS and/or ruxolitinib is stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be other risks that are unknown at this time. There may be a risk of death. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.



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Should death occur, irrespective of the cause, permission for an autopsy will be requested of your family. This is important so that the researchers can further document the safety and effectiveness of this treatment. The researchers encourage you to talk to your family regarding this issue.

Genetic Testing Risks

This study involves testing your DNA, which is the genetic information you inherited from your parents (also known as genetic testing). This testing may include whole genome sequencing (mapping your entire genetic code). Whole genome sequencing generates a large amount of information that may provide, now or in the future, important insights into your health as well as the health of your biologic family members.

If a researcher finds that results from the genetic testing performed on your samples may be useful for your health care, you may be contacted and given the choice to learn the test results. At this time, you will be given general information on the potential risks, benefits, and costs of choosing to learn the test results. The risks of learning genetic test results may include emotional upset, insurance or job discrimination, and/or changes in family relationships because test results may affect other blood relatives. No genetic test results will be put into your medical record unless you choose to learn the results of the testing. Sometimes results should be released only through a genetic counselor who can help explain the possible risks and benefits of learning this information, as well as what these results could mean for you and your family.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest
- If you don't follow the study procedures
- If the study is stopped

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.



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We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

What are the possible benefits from being in this research study?

This study may not make your health better. However, the information learned from the results of this study may help benefit others.

What alternative do you have if you choose not to participate in this research study?

You do not have to be in this study to receive treatment for your condition. Your other choices may include:

- Other standard chemotherapy medications
- Enrollment in a study using other investigational drugs
- No treatment

You should talk to the researcher and your regular physician about each of your choices before you decide if you will take part in this study.



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What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for any tests and procedures which are done just for this research study. These tests and procedures are:

- Tests of immune function
- Blood levels, urine and mouth swabs to check levels of VSV-hIFN β -NIS
- The virus and its administration (VSV-hIFN β -NIS)
- OPTIONAL NIS imaging by TFB-PET scans including the administration of the isotope (TFB) – if done
- Additional biopsies just for research
- And your stay in the hospital to receive the VSV-hIFN β -NIS

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular medical care including routine blood testing, routine monitoring of your cancer by imaging or biopsy, etc.

You may also be billed for other expenses such as medication prescribed at the time of discharge after receiving the virus. If it is needed, Mayo will pay for the use of a specific antiviral agent known as ribavirin that might be used if you develop severe illness due to the administration of the virus.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will not be paid for being in this study. However, hotel reimbursement is provided. The maximum *per diem* for food and hotel will be \$300. Itemized receipts are required. You may be reimbursed for travel to and from the study site for any study visit that you attend. For ground travel using your own car, your reimbursement for travel is based on the round trip number of miles you travel from your home or hotel address to the site address and back as determined by a web-based mileage calculator (e.g., MapQuest).

This distance (miles) will be documented in your study file. You will receive automobile reimbursement per mile at the current IRS mileage rate.



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Your participation in this research study may contribute to the development of commercial products from which Mayo Clinic or others may derive an economic benefit.

You will have no rights to any patents or discoveries arising from this research, and you will receive no economic benefit.

Will your information or samples be used for future research?

We would like to keep your sample for future research. You can still take part in this study without giving permission to use your sample for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Please read the following statements and mark your choices:

1. I permit my sample to be stored and used in future research of cancer at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____ Date: _____

2. I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____ Date: _____

3. I permit Mayo Clinic to give my sample to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____ Date: _____



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There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form. Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

It is possible that information identifying your samples, or your data could be removed. These samples and data will no longer be linked to you. If that were to happen, the samples and data could be used for future research studies or given to another researcher without asking for your permission.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

Various methods are used to safeguard confidentiality. Some or all of the following may be used in this study: assigning a specific code or registration number to each participant's data and samples, research materials stored in locked areas, password protected data stored on a computer.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.



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Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- The sponsor(s) of this study and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.



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Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.



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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

	/	/	:	AM/PM
Printed Name	Date		Time	

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/	/	:	AM/PM
Printed Name	Date		Time	

Signature