INSTITUTE: National Cancer Institute

STUDY NUMBER: 18-C-0137 PRINCIPAL INVESTIGATOR: Mark Gilbert, MD

STUDY TITLE: Phase II Study of Sunitinib in Sarcomas of the Central Nervous System

Continuing Review Approved by the IRB on 06/16/20
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Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Why is this study being done?

The purpose of this study is to find out what effects, good and/or bad, the drug sunitinib malate (referred to as sunitinib) will have on you and your gliosarcoma or sarcoma of the central

nervous system. Sunitinib has been approved in many countries for treating other types of rare or advanced cancers such as kidney, pancreas, stomach and bowel cancer but it is experimental in the treatment of your cancer.

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

You are being asked to take part in this study because you have been diagnosed with a rare cancer (gliosarcoma or central nervous system (CNS) sarcoma) which is eligible for this treatment.

How many people will take part in this study?

This study is being conducted at the National Cancer Institute and it will have three groups: 1) patients with primary gliosarcoma; 2) patients with secondary gliosarcoma; 3) primary CNS sarcoma. Each group will enroll 32 patients for a total of 96 patients. Depending on the results, the study may expand to a second stage and enroll more patients.

Description of Research Study

This study is being conducted on an outpatient basis. Sunitinib is a pill taken once a day, in the morning, with or without food. Sunitinib is stored at room temperature. The dose for this study is 50 mg of sunitinib daily for two weeks, followed by 1 week off with no sunitinib. This 3-week period is called a cycle. During each cycle, you will return to the clinic for certain study-related tests (see Study Chart below for details).

This research study also includes an option to share information about your physical activity levels and the quality of your sleep, because tiredness and lack of energy are risks of sunitinib. If you agree to this optional study procedure, you will be asked to wear, a small, portable watch-sized accelerometer device (called an "Actigraph") on your wrist. The Actigraph device will monitor your overall physical activity levels and sleep patterns throughout six cycles of treatment.

What will happen if you take part in this research study?

Before you begin the study

Before any study-related procedures are performed, you will be asked to read and sign this informed consent form. If you wish to participate, you agree to return to this clinic for all study-related appointments and tests mentioned below. Additional visits may be required to assess and treat side effects. No overnight hospital or clinic stays are required; however, if serious side effects occur, overnight hospital stays may be required to treat the side effects.

You will need to have the following screening exams, tests or procedures to find out if you can be in the study. These tests are part of regular cancer care and may be done if you do not join the study. If you had some of these recently, you may not need to repeat them. This will be up to your study doctor.

- Complete medical history, physical exam (including neurological exam, height, weight)
- Monitor blood pressure and vital signs
- Documentation of all prescription and over-the-counter medications which you are taking
- Standard blood tests (including blood cell counts and chemistries)
- Cranial imaging (CT or MRI) to locate and measure your tumor
- Tissue block and/or unstained slides of the cancer to submit to the study doctor or a member of the research team
- An electrocardiogram (ECG), a recording of the electrical activity of your heart
- An echocardiogram, an ultrasound study which shows the structure and function of your heart
- Serum pregnancy test, for women of child-bearing potential

During the study

During the first three weeks of treatment (cycle 1), you will return to the hospital twice (on days 1 and 8) for study procedures (see **Study Chart** below). Afterwards, you will need to return to the hospital for a clinic visit with your care team once every three weeks. The purpose of each clinic visit will be to monitor your progress on this trial, manage any side effects you may experience, and decide if you should continue this treatment.

While on study, you will take Sunitinib 50 mg by mouth daily for two weeks on (days 1-14) and then one week of rest (no Sunitinib on days 15-21). You will pick up your Sunitinib medication at the NIH Pharmacy at no cost to you.

You will also need to take your blood pressure at home weekly while on this study. The study team will give you a diary to keep track of each dose of Sunitinib and each blood pressure reading. At the end of each cycle, you will bring the completed diary to each clinic visit so you can review it with the research team.

After completing 2 cycles of treatment, you will return to clinic for imaging (MRI or CT scan). This test is needed to determine if the treatment is helping to shrink your tumor. Imaging will be

scheduled every 6 weeks until end of treatment. At each visit prior to imaging, you will also be asked to complete a questionnaire rating your quality of life. This survey takes about 5 minutes to complete.

The treatment cycle may be repeated for as long as you are receiving benefit from the drug (and any side effects you experience are bearable). Once you stop getting any benefit from the study drug, or the side effects are no longer tolerable, we will stop the treatment.

When you are finished taking the drugs (treatment)

Approximately one month after your last dose of Sunitinib, you will return for a final study visit. During this clinic visit, you will have a physical exam with a health care provider, blood work and imaging (MRI/CT scan). See **Study Chart** for details. You will be asked to return the Actigraph device and any medication diaries to the study team.

Study Chart

Day	What to do and what will happen to you
Before starting study	• Check-in to the Outpatient Clinic • Complete medical history and physical exam (including neurological exam and vital signs) by a Health Care Provider • Routine blood tests • Research blood tests • A baseline cranial MRI/CT scan • Questionnaire about your quality of life
During treatment	• Clinic visit– monitor vital signs, review medical history and physical exam by a Health Care Provider* • Routine blood tests* • Research blood tests* • Begin Sunitinib 50 mg by mouth daily for two weeks (days 1-14) • Maintain a medication diary every day (days 1-21) • Monitor your blood pressure at home weekly • Cranial imaging test (MRI or CT scan) after cycle 2 (and then every 6 weeks for as long as you receive the study medication) • Complete a questionnaire about your quality of life • Replace battery on actigraphy device, optional assessment *During Cycle 1, these procedures will occur on day 1 and day 8; all other cycles only on day 1
After treatment	Approximately 30 days after last dose of study drug: • Clinic visit –physical exam by a Health Care Provider • Monitor vital signs and weight • Routine blood tests including thyroid function tests • Research blood tests

	• MRI/CT scan and MDASI survey • Return Actigraphy device, if applicable

Birth Control

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for two months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once. It is also important to note that treatment with sunitinib may make men and women unable to have children in the future.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

Risks or Discomforts of Participation

What side effects or risks can I expect from being in this study?

Studies have shown high blood pressure to be one common side effect of sunitinib. Your blood pressure will be closely watched while you are taking sunitinib. This will include having you check your blood pressure at home on a weekly basis for the entire study. If you have high blood pressure while taking sunitinib, your study doctor may recommend follow-up with your primary care physician and/or starting or increasing medication to lower blood pressure.

Sunitinib may affect how different parts of your body work, such as your liver, kidneys, heart, thyroid and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

Blood Draws

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Questionnaires

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. The primary use of the information you provide is to assess the severity of your symptoms. Submission of this information is voluntary. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the Principal Investigator.

Sunitinib side effects

There is also a risk that you could have side effects from the study drug/study approach. You can make side effects less of a problem by telling the study team if you notice or feel anything different so they can see if you are having a side effect. The study doctor may adjust the Sunitinib dose to try to reduce the side effects.

The list below shows the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

This study may involve unpredictable risks to the participants including death.

Likely side effects (>10%) seen in people taking sunitinib include the following:

- Feeling tired, lack of energy, dizziness
- Frequent or excessive bowel movements
- Stomach treatment-related symptoms: nausea, vomiting, diarrhea, stomatitis, indigestion, decreased appetite, changes in taste (or complete lack of taste)
- Hand and Foot syndrome (redness, pain, swelling or peeling of the palms of the hands or soles of the feet)
- High blood pressure requiring medical intervention
- Low Blood Sugar
- Inflammation of the sinuses and nose (mucosal inflammation)

- Low platelet counts that could cause bruising or bleeding
- Low red blood cell count (anemia) that may result in feeling tired or short of breath and may require blood transfusion
- Low white blood cell count (neutropenia) that could increase the risk of infection
- Skin and hair changes (skin may become yellow, skin/hair may be lighter)
- Skin changes (dry skin, skin thickening or cracking)

Less likely side effects (<10%) seen in people taking sunitinib include the following:

- Abnormal liver function
- Inflammation of pancreas that may show up as upper belly pain that may move to the back, nausea and vomiting that feels worse when eating
- Inflammation of the liver that may show up as yellowing of the skin and whites of the eyes, fever and belly pain
- Thyroid problems
- Wounds that are slow to heal or do not heal
- Damage to the jawbone which may cause loss of teeth
- Kidney damage which may require dialysis
- Blot clot to lungs which may cause shortness of breath, pain, loss of consciousness

Rare and serious side effects (<1%) seen in people taking sunitinib include the following:

Please note that some of these events have been previously stated above, so some have occurred more frequently but with less severity.

- A tear or hole in the intestines which may require surgery
- Belly pain
- Blot clot to lungs which may cause shortness of breath, pain, loss of consciousness
- Bleeding/bruising
- Bleeding in brain

- Change in heart rhythm
- Diarrhea
- Disease progression
- Decreased white blood cells, red blood cells, and/or platelets which may manifest with fever, feeling cold, infections, shortness of breath, feeling tired, a tendency to bruise easily, or a tendency to bleed easily
- Fatigue
- Fever
- Gastrointestinal stromal tumor
- Hand and Foot syndrome (redness, pain, swelling or peeling of the palms of the hands or soles of the feet)
- Heart attack or heart failure which may cause shortness of breath, swelling of ankles and tiredness
- Kidney failure which may require dialysis
- Liver failure
- Loss of body fluid manifesting as feeling tired, confused, having a dry mouth, or feeling thirsty (dehydration)
- Low white blood cell count (neutropenia) that could increase the risk of infection
- Multi-organ failure
- Nausea
- Flesh eating bacteria syndrome
- Pneumonia
- Respiratory failure
- Brain damage which may cause headache, seizure, blindness, high blood pressure, decreased alertness, blindness (also known as reversible posterior leukoencephalopathy syndrome (RPLS))
- Sepsis

- Severe skin rash with blisters and peeling which can involve the mouth and other parts of the body
- Shortness of breath
- Tumor lysis syndrome (Tumor cells spread to blood stream and cause complications)
- Vomiting

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to see if Sunitinib will cause your tumor to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Alternative Approaches or Treatments

What other choices do I have if I do not take part in this study?

Instead of being in this study, you have these options:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

Stopping Therapy

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment

- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if you become pregnant

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Pfizer and Clinical Director or Deputy Clinical Director, CCR, NCI or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.

There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.

Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.

Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Cancer Institute Institutional Review Board
- Qualified representatives from Pfizer, Inc., the pharmaceutical company who produces Sunitinib.

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.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this

research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

Pfizer Inc. is providing Sunitinib for this study to NIH without charge. No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested. However, there are some non-NIH collaborators on this study who may receive payments or benefits, limited by the rules of their workplace.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Mark Gilbert, M.D., Building 82, Room 235A, Telephone: 240-760-6023. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative — Date

Print Name

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.

(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian — Date

Print Name

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian — Date — Print Name

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JUNE 16, 2020 THROUGH JUNE 15, 2021.

Signature of Investigator — Date

Print Name

Signature of Witness — Date

Print Name