INSTITUTE: National Cancer Institute

STUDY NUMBER: 17-C-0088 PRINCIPAL INVESTIGATOR: John Glod, M.D., Ph.D

STUDY TITLE: A Phase II Trial of the DNA Methyl Transferase inhibitor, SGI-110 (Guadecitabine), in Children and Adults Wild Type GIST, Pheochromocytoma and Paraganglioma Associated with Succinate Dehydrogenase Deficiency and HLRCC-Associated Kidney Cancer

Continuing Review Approved by the IRB on 02/11/19
Amendment Approved by the IRB on 11/5/19 (B) Date Posted to Web: 11/14/19

Assent

We would like to invite you to take part in a research study at the National Institutes of Health (NIH). Before you decide about taking part in the study, we want you to know why we are doing the study and if it will help you. We also want you to know about any risks (what might go wrong) and what you will have to do. You can only be in the study if you and your parent(s) agree.

This form gives you information about the study. Your doctor will talk to you about the study and answer questions you have. If you would like to take part in this study, we will ask you to sign this form to show that you understand this study. We will give you a copy of this form to keep. It is important that you know:

- You do not have to join the study.
- You may change your mind and drop out of the study at any time.

If we make important changes to the study we will tell you about it and make sure you still want to be in the study.

Why is this study being done?

You are being asked to take part in this study because you have one of the following 3 disorders:

- Gastrointestinal stromal tumor (GIST) that does not have certain mutations;
- Pheochromocyteoma and paraganglioma or
- Kidney cancer related to a disorder called hereditary leiomyomatosis and renal cell carcinoma.

You will only be eligible for this trial if the other known treatments for your disorder, such as surgery, radiation therapy or chemotherapy, have not worked for you.

The purpose of this study is to learn if SGI-110, an experimental drug, causes your tumor to shrink or grow less quickly and to study how SGI-110 acts in the body (pharmacokinetics, also known as PK).

What will I be asked to do? What are my requirements?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer, such as physical examination, laboratory testing and scans and x-rays. However, there are some extra tests.

Before you begin the Study

You will have these extra tests to find out if you are eligible to participate in the study:

- Tests to make sure you are not pregnant (if you are a female and old enough to become pregnant)
- CT or MRI Scan of your tumors

During the Study

Treatment on this study will require you to come to clinic each day for 5 days in a row. You will receive an injection under your skin, usually in the belly of the study drug SGI-110. This will occur every 28 days (called a cycle) for as long as you tolerate the drug and if it is effective.

Medical Tests During Treatment

Whether you are on this study or not the following medical tests will be done to monitor for response to treatment as well as side effects related to treatment. These include:

- Physical exam including checking your blood pressure, pulse, breathing, height and weight
    - Blood tests to check how well your organs are working and to make sure you are not pregnant if you are a female old enough to become pregnant
- Tumor evaluation that may include a CT or MRI scan

You will have regular medical appointments throughout treatment.

Tests for research purposes

In addition to the routine tests listed above, we would like to do other tests while you are enrolled on the study.

Questionnaires

These will be used to find out how, if at all, SGI-110 affects your pain and quality of life. You will complete two questionnaires that take about 10 minutes each to complete before you have taken any SGI-110 and then at the end of cycle 4, and then every 4 cycles thereafter, and at the time you stop SGI-110 treatment. T

SGI-110 Drug Levels (Pharmacokinetics)

About a 1/2 teaspoon will be collected before your first dose of SGI-110 and then after the first dose at ½ hour, 1, 2, 4, 6, and 24 hours after the first dose. Any leftover blood that is not used for this test will be destroyed.

Pharmacodynamics (called PD studies) to study the effects of SGI-110

- We will ask for a urine sample and for about a ½ teaspoon of blood.

Final Study Visit

At the end of treatment with SGI-110 you will have an evaluation at the NIH which will include a final evaluation of your pain and quality of life.

What bad effects can happen by being in the study?

This study drug may make you sick. You may feel tired, have swelling and redness at the site where the drug is injected, and you may bruise or bleed.

This drug can also lower the number of your red blood cells, which carry oxygen to your body. When your red blood cells are low, you may feel tired or have a headache or feel dizzy.

You may experience diarrhea with this drug and should record the number of stools and associated symptoms. If you develop diarrhea you should inform the study doctor. The study doctor may give you a dose of medicine after the first time you have an unformed, loose stool. The doctor may decide to continue this medicine until you have not had diarrhea for at least half a day. If your diarrhea gets worse or if you start to vomit, have a fever, your belly hurts or you have nausea and can't keep liquids down you should call the study doctor or the study nurse.

In rare cases, you may have swelling of the eye or face. You may also have kidney damage and when the kidneys do not work properly, wastes can build up in your blood. This could become severe, requiring dialysis to clean the wastes out of your blood.

This study drug may be harmful to an unborn child. Birth control measures should be used by all girls in this study who can become pregnant and are sexually active. Sexually active boys in this study should also use birth control measures to prevent their partners from becoming pregnant. These birth control measures can include not having sex, contraceptive pills, or use of condom and spermicide cream.

We will let you know about any new findings during the study, which may change your willingness to continue to participate in the study.

What benefit can I expect?

The study drug that you will receive could make your tumor(s) shrink or stop growing for a period of time. However, we do not know how likely it is that your tumor(s) will shrink or stop growing for a period of time or that you will benefit from this treatment. Information from this study will help us find out if this treatment will help patients with y.

Can I refuse to be in the study?

Participation in this study is purely voluntary. We will discuss with you and your parents/guardian about the various options for therapy if you do not want to be in this research study. Each alternative therapy has a unique set of benefits and risks and your doctor will discuss these options with you.

You will not be paid for any part of your participation in this study. Participating in this study will not cost you or your parents any money.

We will keep the records of this study confidential. Only people working on the study at your site will know your name. Your name will not appear on the study forms. Instead, you will be assigned a patient identification number.

You may stop being in this any time

Remember, being in this study is up to you and no one will be upset if you don't want to take part in this study or even if you change your mind later and want to stop.

Re-consenting

Once you have turned 18, we will contact you to find out if you would still like to participate in the study.

You can ask any questions that you have about the study.

If you have a question later that you didn't think of now, you can call me at 240-760-6194 or ask me next time you see me. You may call me at any time to ask questions about your disease and treatment.

Putting your name at the bottom means that you have decided to be in this study. You and your parents will be given a copy of this form after you have signed it.

I have had this study explained to me in a way that I understand, and I have had the chance to ask questions. I agree to take part in this study.

Signature of Minor Patient:_____Date:_____

Print Name:_____

Signature of Investigator:_____Date:_____

Print Name:_____