

<b>MEDICAL RECORD</b>	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> <ul style="list-style-type: none"> <li>• Adult Patient or</li> <li>• Parent, for Minor Patient</li> </ul>
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INSTITUTE: National Cancer Institute

STUDY NUMBER: 13-C-0208      PRINCIPAL INVESTIGATOR: Brigitte Widemann, M.D.

STUDY TITLE: Phase II Trial of Vandetanib (ZD6474, Caprelsa<sup>®</sup>) in Children and Adults with Wild-Type Gastrointestinal Stromal Tumors

Continuing Review Approved by the IRB on 12/03/18

Amendment Approved by the IRB 12/06/17 (F)

Date posted to web: 12/13/18

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.

If you are signing for a minor child, “you” refers to “your child” throughout the consent document.

### Why is this study being done?

You have been diagnosed with Gastrointestinal Stromal Tumor (GIST), wild type, called WT-GIST. We have found that some people with WT-GIST have a mutation (or change) in one of their genes. Some cancer agents have successfully treated diseases with a similar gene mutation. Vandetanib is one cancer treatment that has been recently approved by the US Food and Drug

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Administration (FDA) for treatment of adults with medullary thyroid cancer, but has not been previously given to people with your type of cancer, and is therefore considered experimental. The purpose of this study is to test whether vandetanib will benefit people with Wild-type GIST.

Vandetanib is a pill that is to be taken once a day. The purposes of this research study:

- to see if Vandetanib can shrink tumors in people with wt-GIST.
- to test the safety and tolerability of vandetanib in children and adults, and to see if it prolongs survival.
- to study if a scan (FDG-PET scan) is helpful in evaluating patients who are 15 years of age or older with wt-GIST,
- to study tumor cells from patients with wt-GIST to better understand the biology of the disease, and
- to describe the impact of taking vandetanib on your quality of life and symptoms if you are 8 years of age or older.

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

You are being asked to take part in this study because you are 3 years of age or older and have been diagnosed with wild-type GIST.

**How many people will take part in this study?**

A minimum of 9 and a maximum of 24 patients will be enrolled in this study.

**Description of Research Study****What will happen if you take part in this research study?**

*Before you begin the study*

First we will test your tumor tissue to make sure it is the wild-type GIST. If it is wild-type GIST, you will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- A medical history
- Physical exam
- Vital signs (blood pressure, pulse, temperature, height and weight)
- Standard blood tests
- Electrocardiogram (ECG), which is an electrical recording of your heart
- Pregnancy test (if you are a female who could have children)

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- Scans of the tumor (CT and MRI) or other tests needed to check the status of your tumor.

For your safety and to get valid study results, your test results must be within the limits outlined for eligibility to participate in this study. Your study doctor will tell you if you are eligible for this or another study.

The effects of the drug used in this study on an unborn child (fetus) are unknown. For this reason, if you are pregnant or nursing, you may not participate. You/your partner must be willing to use an effective form of contraception (hormonal or barrier method of birth control, or commitment to sexual abstinence) prior to your entering this study and for 3 months after you finish vandetanib on this study. If you or your partner becomes pregnant while you are participating in this study, you should notify your doctor immediately. Women who are able to get pregnant must have a negative pregnancy test.

**Note:** it is *very important* for you to give the researchers *accurate* and *complete* information about your medical history and condition.

*During the study*

Prior to starting vandetanib, you will have standard tests to allow us to watch for any changes while you are taking vandetanib. The following standard tests will be done:

- Routine blood tests including thyroid function, liver function, and chemistries.
- Routine urine testing
- Scans, including MRI, CT and FDG-PET
- If you are younger than 18 years old, lower extremity x-ray to check bone growth.
- If you are 8 years of age or older (and all parents or caregivers) complete questionnaires about quality of life.

You will take vandetanib once every day continuously (a cycle of vandetanib is 28 days).

Adults will receive 200 mg every day for the first 3 cycles, which has been shown to be safe in adult studies. If you tolerate this dose, the dose may be increased to 300 mg every day.

Children will receive a dose based upon weight and height starting at 100 mg/m<sup>2</sup>/dose for cycles 1, 2 and 3. If this dose is tolerated, the dose will be increased to 150 mg/m<sup>2</sup>/dose for subsequent cycles.

Taking vandetanib is not affected by food so you do not need to take it when you eat, but it should be taken about the same time every day.

The tablet should be swallowed whole or dissolved in water. If you miss a dose of vandetanib and less than 12 hours have passed since the scheduled dose, you should take your dose immediately. If more than 12 hours have passed, then do not take the missed dose but wait and take the next scheduled dose the next day.

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If you vomit within 30 minutes of taking vandetanib, then you can take another dose. The dose may only be repeated once. If more than 30 minutes has passed since you took the dose, then do NOT repeat the dose. Take the next scheduled dose the next day.

We will ask you to write down the dose of vandetanib and the time and date you took it every day in a medication diary. Make sure you bring your medication diary with you to every clinic visit.

If you have side effects with vandetanib, be sure to discuss them with your doctor or nurse. You may be given medications to make you feel better, or the dose may need to be adjusted. DO NOT take other medications without first discussing them with your doctor or research nurse.

During the first 28-day cycle, you will be examined by a doctor at the NIH or at home at about day 14 of the cycle to look for side effects of vandetanib.

After the first cycle you will need to have a physical exam, urine tests, blood pressure checked and routine blood tests before cycles 2, 3, and 4. These tests will then be done periodically for as long as you are on the study. Procedures or tests that need to be done by your own physician at home will incur costs that may or may not be covered by your health insurance.

The effect of vandetanib on your cancer will also be closely monitored while you are on the study:

- scans to assess the size of your cancer (may include CT scan and MRI) will be done before cycle 4 and then every 3-6 cycles, and
- FDG-PET will be done before cycle 4, and then again only if the doctor thinks you need it.

If you are female and able to have children, a urine or blood pregnancy test will be done prior to starting cycles 4, 7, 10, and 13 of vandetanib and then every 6 cycles while you are taking the study drug.

If you are still growing (children and adolescents) we will do an MRI of your knee to see if your bones are still growing. If so, you will need to have an MRI periodically during your participation in this study to see any side effects on your growing bones.

You may continue to receive vandetanib indefinitely unless you decide to stop for any reason, you have unacceptable side effects that are not controlled by lowering the dose, your tumor grows, you are unable to keep scheduled medical appointments or take the study medication as instructed, the doctors taking care of you feel it is not in your best interest to continue, or a better therapy becomes available.

If you become pregnant you will need to stop taking vandetanib. While you are being treated with vandetanib, doctors at the NIH will provide you with any new information that develops which may affect your health, welfare, or willingness to stay on the study.

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NIH-2514-2 (10-84)

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Quality of Life (QOL) Questionnaires and other Optional Tests (if you are 8 years of age or older)

We will offer you participation in some tests that include Quality of Life Questionnaires, tissue tests in case a biopsy or surgery is clinically necessary, and imaging studies (PET-CT). They are all described at the end of this informed consent.

*When you are finished taking the drugs (treatment)*

If you come off the treatment for any of the reasons listed above, we would like you to return to NIH for one visit about 60 days after your last dose of vandetanib for a physical exam and standard blood tests. We will continue to check up on your condition periodically through phone calls to you, your family or your home doctor’s office.

**Study Chart**

Cycle 1		Subsequent Cycles	
DAY	WHAT YOU DO	DAY	WHAT YOU DO
Before starting study	<p><b>Come into the clinic and do the following:</b></p> <ul style="list-style-type: none"> <li>• Get routine blood tests</li> <li>• Get an ECG</li> <li>• Get a pregnancy test (if you are a female able to get pregnant)</li> <li>• Get a physical exam by your doctor (including blood pressure, heart rate, weight, temperature)</li> <li>• Get a disease evaluation (CT and MRI) that will be done by your doctor.</li> </ul> <p><b>If you are able to be in the study, you will have:</b></p> <ul style="list-style-type: none"> <li>• FDG-PET scan</li> <li>• Urine tests</li> <li>• MRI of your lower leg if you are still growing</li> <li>• QOL questionnaires (if you are 8 years of age or older)</li> </ul>		
Day 1	<p><b>Come into the clinic:</b></p> <ul style="list-style-type: none"> <li>• Get a physical exam by your doctor, check blood pressure</li> <li>• Get a Patient Diary that you will need to write in daily</li> </ul>	Days 1-27	<ul style="list-style-type: none"> <li>• Take vandetanib once a day</li> <li>• Write the dose in your Patient Diary daily</li> </ul>

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	<ul style="list-style-type: none"> <li>Start taking vandetanib once a day for 28 days, continuously without interruption</li> </ul>		
Day 2 thru 27	<ul style="list-style-type: none"> <li>Take your vandetanib once a day</li> <li>Write the dose in your Patient Diary daily</li> <li>[<sup>18</sup>F]-FDG-PET/CT scan between day 3-6 after starting vandetanib (optional if you are older than 15 years of age)</li> </ul>		
Also on Day 15	<ul style="list-style-type: none"> <li>Get a physical exam, check blood pressure</li> <li>Get routine blood tests</li> </ul>		
Day 28	<p><b>Come into the clinic:</b></p> <ul style="list-style-type: none"> <li>Get a physical exam by your doctor</li> <li>Get blood pressure measurement</li> <li>Get an ECG</li> <li>Get routine blood tests</li> <li>Get urine test</li> <li>Get a pregnancy test (if you are a female able to get pregnant)</li> <li>If continuing treatment, get vandetanib for the next cycle and a new Patient Diary to write in daily</li> </ul>	Day 28	<p><b>Come into the clinic:</b></p> <ul style="list-style-type: none"> <li>Get a physical exam with blood pressure by your doctor (before cycles 2, 3 and 4, then every 3 cycles (7, 10, 13))</li> <li>Get an ECG (before cycles 2, 3, and 4, and then every 3 cycles, i.e. 7, 10, 13)</li> <li>Get routine blood and urine tests (before each cycle for cycles 2, 3 and 4, then every 3 cycles (before cycle 7, 10, 13).</li> <li>Get a pregnancy test (if you are a female able to get pregnant) (before cycles 4, 7, 10, 13, then every 6 cycles, i.e. 19, 25, 31)</li> <li>If continuing treatment, get vandetanib for the next cycle and a new Patient Diary to write in daily</li> <li>Evaluate tumors with CT and MRI every 3 cycles (before cycle 4, 7, 10 and 13) then every 6 cycles (19, 25, 31, etc)</li> <li>FDG-PET scan before cycle 4, then if your doctor sees a need.</li> </ul>

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			<ul style="list-style-type: none"><li>• <b>QOL questionnaires (if you are 8 years of age or older) before cycle 4, and then when you stop taking vandetanib</b></li></ul>
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**Risks or Discomforts of Participation**

The study medication may cause some side effects. Depending on the severity of the side effect, the dose of vandetanib may need to be decreased, or stopped.

The following side effects were observed in patients receiving 300mg vandetanib alone (with no other treatment). Vandetanib may involve other risks, including possible life-threatening reactions that are not known at present. You may experience some, none, or all the possible side effects of vandetanib. The side effects most likely to occur are:

**Very common – experienced by more than 10% of patients taking vandetanib:**

- headache
- diarrhea
- fatigue
- nausea and/or vomiting
- constipation
- loss of appetite
- skin rash or dry skin
- weight loss
- trouble sleeping
- high blood pressure, or
- weakness.

**Patients taking vandetanib may develop a skin rash that may become severe but is manageable with proper treatment. Vandetanib may also make your skin more sensitive to the sun.** It is recommended that you take preventative action to prevent the rash from occurring while receiving study medication and for 3 to 4 weeks after stopping treatment by using the following guidelines:

- Avoiding direct sunlight
- Covering sun exposed skin with clothing (long pants, long sleeve shirts and hats)
- Using a SPF 45 or higher sunblock or sun protection cream
- Notifying study doctor when the first sign of a rash occurs so he or she may take the appropriate steps in preventing the rash from becoming severe

**Common (Experienced by 1 – 10% of patients taking vandetanib)**

- Changes in heart function (called QTc prolongation), abnormal taste in mouth, abdominal pain, swelling in your mouth, dry mouth, decrease in thyroid hormone, weight loss, elevated blood levels of certain proteins produced by the liver, anorexia, low potassium in the blood, low calcium in the blood, dehydration, low magnesium in the blood, changes in your skin (sensitivity to the sun, itchy skin, redness), acne, hair loss, nail disorders, mild nose bleeding, protein or blood in the urine, kidney stone, changes in your eyes (vision problems, swollen, dry or irritated eyes), feeling depressed, and anxiety.
- AstraZeneca, the company that makes Vandetanib, has observed changes in ECGs in some patients being treated with vandetanib. These changes in the ECG may be drug-related and usually occur without symptoms. Similar changes in the ECGs of patients receiving other medications have led to heart rhythm changes, some of which have been life threatening. It is estimated that between 0.1 to 1% of patients receiving vandetanib 300 mg have developed heart rhythm changes linked to life-threatening arrhythmia called Torsades de Pointes. Torsades de Pointes has been associated with sudden death. If any such changes are noted on your ECGs, you may need to attend additional visits for further safety assessments.
- The risk of developing changes in the ECG and serious heart rhythm changes will be greater if you have diarrhea, imbalance of minerals in your blood, vomiting, high fever, faintness or dizzy spells, or are unable to maintain a normal diet. You should report any of these symptoms to your study doctor immediately. You should review your medications and diet with your study doctor at each visit while you are continuing to receive study drug.
- Changes in the heart rhythm may cause rapid or irregular heartbeat, dizziness, light-headedness, chest discomfort, shortness of breath, or losing consciousness. We will be checking your heart function with an electrocardiogram (ECG). If significant changes occur, we may need to stop therapy. These or other new symptoms or possible side effects should be reported immediately to your study doctor.



**Uncommon (Experienced by fewer than 1% of patients taking vandetanib)**

- Certain heart conditions (heart failure – a weakening of the heart's ability to pump blood, a fast heart beat that can be dangerous), chest pain, inflammation in the pancreas, decrease in platelets in the blood, small bluish/purple spots on the skin, increase in haemoglobin in the blood, and severe skin disorders.
- Some patients have had seizures while taking vandetanib, which can be a result of swelling in the brain. This can be seen on an MRI scan, and is expected to improve after vandetanib has been stopped. If you develop seizures, dizziness, headache, changes in your vision, or confusion, you should let your study doctor know as soon as possible. These may be symptoms of reversible posterior leukoencephalopathy syndrome (RPLS) which is expected to be uncommon.
- A very small number of patients with lung cancer receiving vandetanib have developed shortness of breath and cough because of an inflammation of scar tissue formation in the lungs, although this symptom could also be due to the underlying lung cancer.

**Women of Child-Bearing Potential and Men with Partners of Child-Bearing Potential**

There might be unknown risks to the unborn baby if you are or if you become pregnant during the study. Due to these risks, you must not take part in this study if you are pregnant, plan to become pregnant during the research study period, or are breast-feeding a baby.

**If you are a woman of child-bearing potential:**

- By signing this consent form, you confirm to the best of your knowledge that you are not pregnant now and you do not intend to become pregnant during this study
- A pregnancy test will be done to confirm that you are not pregnant before you take part in this study
- You must avoid becoming pregnant and use an acceptable method of birth control during your participation in this study. An acceptable method of birth control is defined as a barrier method in conjunction with a spermicide (i.e., condom with spermicide, diaphragm with spermicide), approved contraceptive implants, long-term injectable contraception, intrauterine devices, or tubal ligation. The oral contraceptive pill is acceptable, but it must be combined with a barrier method in conjunction with a spermicide. You should avoid becoming pregnant for 3 months following the last dose of vandetanib.

If at any time during this study you think you might be pregnant, or later learn that you were pregnant during the study, you must contact the study doctor immediately for further instructions about your participation in this study and follow-up. You will be asked about the results of the pregnancy/birth and may need to have follow-up visits.

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**If you are a man with a partner of childbearing potential, then you must immediately contact the study doctor if any of the following occur:**

- Your partner becomes pregnant during the study
- You learn that your partner became pregnant during the study
- You learn that your partner became pregnant within 3 months after your last dose of the study drug.

You will be given further instructions for follow-up.

Male patients must avoid unprotected sex with a pregnant partner (or woman of child-bearing potential not using birth control) or donating sperm during the study and for **three months** following the last dose, since the potential for problems with the fetus has not yet been thoroughly investigated. Men should use a condom during the trial and for **three months** following the last dose.

The study doctor may ask you about any partner pregnancy during your study visits, and again up to 3 months after the last dose of study drug. If you report a pregnancy of your partner, the study doctor will collect information about the results of the pregnancy/birth and schedule any follow-up visits that are needed.

This health information will become part of the research study records. It will be shared with the drug manufacturer. With this information, the drug manufacturer may be able to determine if there are any effects of the study drug upon unborn children.

**Additional Risk (not associated with vandetanib, but may be associated with participation in the study):***Drawing Blood*

Taking blood samples may cause some discomfort. Risks associated with drawing blood from your arm include pain, bruising, light-headedness, and on rare occasions, infection.

*Risks of Scans*

You will have a CT scan and MRI to measure the size of your cancer(s) before starting the treatment and some or all of these scans will be used to periodically monitor the change in the size of your cancer(s) on vandetanib. These scans are common standard imaging tests used in the diagnosis and monitoring of many diseases. Although these tests have been in use for many years, their potential long term effects on the body are still being learned.

The most common discomfort is the length of time you must lay still or flat while a scan is being performed. Occasionally, a patient may become uncomfortable within the enclosed space of the scanners (claustrophobia), particularly during a MRI. If this occurs, cool air can be blown over you by a fan if desired or your doctor can order a medicine to help you relax during this scan. Keeping the room well lit can also reduce this claustrophobic feeling.

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If a contrast agent (the special dye) is given with the scan there is a small risk of having a reaction to the contrast. These reactions can include nausea, pain in the vein where the contrast was given, headache, a metallic or bitter taste in the mouth, and a warm or flushing feeling that lasts from 1-3 minutes. Rarely, these symptoms may require treatment. In very rare cases, people have had more severe allergic reactions that result in shortness of breath, wheezing, or lowering of the blood pressure. If you have had a reaction in the past, be sure to tell your doctor or nurse about it.

The radiation dose you receive, if your scans include the use of X-rays or radioactive chemicals, is considered essential for your medical care.

In some cases, you may require medicines to make you sleep so you can be still during the procedure. The risks from this sedation or anesthesia are dependent on the types of medication used. These risks will be fully explained to you prior to the procedure and a separate informed consent will be obtained for anesthesia.

We may need to insert an IV line for administration of the contrast or anesthesia. This can cause pain at the site where the IV is placed and carries a small risk of bruising or infection.

Patients with a cardiac pacemaker, neural pacemaker, some types of surgical clips, ear implants, foreign metal objects, permanent dental retainers, or any iron-containing material within the body should not undergo a MRI, because of the effect of the strong magnet on these objects.

#### *FDG-PET Scan*

FDG-PET Scan, which is a nuclear medicine test also called a Positron Emission Tomography (PET) scan. This is an imaging technique that is used to detect and follow the presence of a variety of tumors. Positron emission tomography (PET) uses a radioactive sugar molecule called fluorodeoxyglucose, or FDG for short. This sugar is similar to glucose, an ordinary form of sugar that the body uses for fuel. The FDG is labeled with a type of radioactive element, an isotope, called Fluorine-18 (F-18) that emits particles called positrons that can be detected by a special camera and viewed on a computer screen. The FDG will be injected into the vein. You will need to be fasting (you will not be able to eat or drink) for 4 to 6 hours before the FDG-PET scan.

There is a slight risk of developing an allergic-type reaction to the radioactive drug, FDG which is given in a catheter put in your vein (intravenously) before the PET scanning is done. There may be discomfort when the needle is put into your arm vein. There is a slight risk of bruising, bleeding or infection at the site of injection. There may be discomfort associated with lying still on the enclosed scanning table.

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**Potential Benefits of Participation****Are there benefits to taking part in this study?**

Vandetanib may cause your cancer to stop growing or shrink in size for a period of time or it may lessen the symptoms, such as diarrhea, that are caused by the cancer. Because there is little information about the drug's effect on cancer in children and adolescents, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may benefit others.

**Alternative Approaches or Treatments****What other choices do I have if I do not take part in this study?**

Alternatives to Vandetanib include:

- conventional drugs that were previously used in the treatment of your cancer,
- other conventional anticancer drugs that are not routinely used to treat your type of cancer,
- other experimental therapies, or
- getting no anticancer treatment but receiving comfort care, also called palliative care. This type of care tries to reduce pain, tiredness, appetite problems, and other problems caused by cancer. It does not treat the cancer directly, but instead 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****Could the researchers take me out of the study even if I want to continue to participate?**

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

- if he/she believes that it is in your best interest
- if you become pregnant
- 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

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 collaborators. 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

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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 AstraZeneca, the pharmaceutical company who produces Vandetanib.

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.

**What Happens if You Have an Injury Resulting from this Study?**

Please see the information in #2 on page 17.

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**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.

Astra-Zeneca is providing the drug for this study to NIH without charge. No NIH investigator involved in this study receives payments or other benefits from any company whose drug,

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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.

**Quality of Life Questionnaires (if you are 8 years of age or older)**

We would like to gather information about the effects of vandetanib on you and your daily life by having you complete a series of questionnaires (2 forms). It will take about 10 minutes to complete the questionnaires. We will ask you to fill them out 3 times. Participation will not benefit you. It might help other people in the future.

**Optional Tissue Research****Archival Tumor Tissue**

We would like to study tumor tissue from people with GIST to learn more about how to prevent or treat GIST. If you have tumor tissue available from a prior biopsy or surgery, we would like your permission to use your previously collected tissue to study these research questions in our laboratory. Participation is optional and will not benefit you. It might help other people in the future. Even if you sign "yes" to allow us to study your tumor tissue, you can change your mind at any time. Please read the sentence below and think about your choice. After reading, circle and initial the answer that is right for you. The decision to participate in this part of the research is optional, and no matter what you decide to do, it will not affect your care.

I agree to allow previously collected tumor tissue to be used for research tests in this study.

Yes          No          Initials \_\_\_\_\_

**Tissue Collected While on this Study**

If you need a biopsy or surgery while you are on this study, we would like to use a small piece of any tumor obtained during the surgery to study any genetic changes present in your cancer. Because your type of cancer is very rare, attempts will be made to grow cancer cells from your tumor cells in test tubes (establishing so-called "cell lines"). Cancer cells taken directly from you have a limited time of survival and cannot be studied in the future. Cells grown under specific laboratory conditions can be made into a *cell line*, which can survive indefinitely, allowing us to study the best ways to diagnose and treat future patients with wt-GIST. These tests are only done for research purposes and will not affect your medical management on this study. Therefore, if you have surgery or a biopsy of your tumor we would like to study your tissue. Participation is optional and will not benefit you. It might help other people in the future. Even if you sign "yes" to allow us to study your tumor cells, you can change your mind at any time. Please read each sentence below and think about your choice. After reading, circle and initial the answer that is right for you. The decision to participate in this part of the research is

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**MEDICAL RECORD****CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

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optional and will not benefit you, and no matter what you decide to do, it will not affect your care.

I agree to allow part of my tumor tissue from a biopsy or medically indicated surgery be used for research tests in this study.

Yes            No            Initials\_\_\_\_\_

**Optional additional [<sup>18</sup>F]-FDG-PET/CT scan**

If you are 15 years of age or older, we invite you to participate in one additional [<sup>18</sup>F]-FDG PET/CT scan (only if you do not require sedation). This scan is optional and is done solely for research purposes and is **not** required for your medical care. This additional scan will be done 3-6 days after you start taking Vandetanib to see if the [<sup>18</sup>F]-FDG PET/CT scan can help us see who will benefit from Vandetanib therapy.

This research [<sup>18</sup>F]-FDG-PET/CT scan involves exposure to radiation from the one [<sup>18</sup>F]-FDG PET/CT scan with an injection of 10 millicuries of F-18 FDG tracer, which is given before the [<sup>18</sup>F]-FDG PET/CT scan. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 1.4 rem in children 15 years old which is above the NIH Radiation Safety Committee guidelines of 0.5 rem per year in children, but the Radiation Safety Committee has approved this scan in patients because of the value of the scientific information we will obtain. The amount of radiation you will receive in this study in adults is 1.1 rem, which is within the NIH Radiation Safety Committee guidelines of 5 rem per year. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care at the NIH or other places/hospitals that use radiation. This way we can make sure that you will not receive too much radiation. Consider X-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

**If you are pregnant or breastfeeding, you will not be permitted to participate in this research study.** It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

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PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent



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**MEDICAL RECORD****CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

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I agree to participate in this research FDG-PET in this study.

Yes          No          Initials \_\_\_\_\_

**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.

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**PATIENT IDENTIFICATION****CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

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**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, Brigitte Widemann, M.D., Building 10, Room 1-5750, Telephone: 240-760-6203. 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.

**MEDICAL RECORD****CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY**

- Adult Patient or
- Parent, for Minor Patient

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**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 DECEMBER 03, 2018 THROUGH DECEMBER 17, 2019.**

\_\_\_\_\_  
Signature of Investigator

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Witness

\_\_\_\_\_  
Date

\_\_\_\_\_  
Print Name

\_\_\_\_\_  
Print Name

PATIENT IDENTIFICATION

**CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY (Continuation Sheet)**

- Adult Patient or
- Parent, for Minor Patient

NIH-2514-1 (07-09)

P.A.: 09-25-0099

File in Section 4: Protocol Consent