PRINCIPAL INVESTIGATOR: Christine Heske, MD

STUDY TITLE: A Phase I/II Trial of the Insulin-like Growth Factor 1 Receptor (IGF-1R) Antibody AMG479 (Ganitumab) in Combination with the Src Family Kinase (SFK) Inhibitor Dasatinib in Patients with Embryonal and Alveolar Rhabdomyosarcoma

STUDY SITE: National Cancer Institute

Cohort: Affected Patient

Consent Version: March 3, 2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator:
Christine Heske, MD
Email: Christine.heske@nih.gov
Phone: 240-760-6197

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being enrolled is a minor then the term "you" refers to "you and/or your child" throughout the remainder of this document.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHAT IS THE USUAL APPROACH TO MY DIAGNOSIS?

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma of childhood. Two major types of RMS are embryonal rhabdomyosarcoma (ERMS) and alveolar rhabdomyosarcoma (ARMS). The treatments for RMS include surgery, radiation therapy or chemotherapy. Some of the agents used to treat rhabdomyosarcoma are approved by the U.S. Food and Drug Administration (FDA) for other indications. New types of treatments being tested in clinical trials include high-dose chemotherapy with stem cell transplant, immunotherapy, or targeted therapy.

The insulin-like growth factor (IGF) system plays an important role in many cancers. Over-expression of the type 1 IGF receptor (IGF-1R) has been observed in sarcoma. An enzyme called YES is also highly expressed in both ERMS and ARMS. Treatment blocking both IGF and YES appears to slow tumor growth of ERMS and ARMS cells studied in the laboratory.

Dasatinib is an enzyme inhibitor that may block over-expression of YES. Dasatinib also appears to have anticancer activity in some cancers. Ganitumab is a monoclonal antibody directed specifically against IGF-1R to suppress tumor growth.

WHAT IS THE USUAL APPROACH TO MY CANCER?

You are being asked to participate in this trial because you have ERMS or ARMS and the other known treatments for your disorder, such as surgery, radiation therapy or chemotherapy, have not proven effective for you. People who are not in a study are usually treated with surgical removal of their tumor, radiation, and/or chemotherapy. You may decide not to receive any treatment directed at shrinking your tumor(s) at this point in time.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

Please talk to your doctor about these and other options.

WHY IS THIS STUDY BEING DONE?

The purposes of this research study are:

1. To find the safe dose of dasatinib when given with ganitumab in patients with ERMS and ARMS.
2. To assess if the combination of ganitumab and dasatinib is helpful in the treatment of your type of tumor(s) (causes your tumor to shrink or slow down the growth), or can increase survival.
3. To study the side effects of the combination of ganitumab and dasatinib.
4. To study how ganitumab and dasatinib act on the tumors of people with RMS.
5. To do genomic analysis of tissue samples of patients with ERMS and ARMS (you will be asked to participate in another POB study for this called protocol 10-C-0086:

Comprehensive Omics Analysis of Pediatric Solid Tumors and Establishment of a Repository for Related Biological Studies)

Ganitumab is being used in clinical studies and has been given to adults and children with different types of tumors. Dasatinib was approved by the U.S. Food and Drug Administration (FDA) for treatment of adults with a type of chronic myeloid leukemia (CML). Ganitumab has not been approved by the U.S. Food and Drug Administration (FDA) for any indication. Ganitumab and the combination of ganitumab and dasatinib are experimental, meaning they have not been approved by the FDA, but are approved for use in this clinical trial.

Up to 24 evaluable patients may take part in this study.

WHAT ARE THE STUDY GROUPS?

All study participants will get the same study intervention. You will take the dasatinib pills by mouth every day. The treatment will be divided into cycles. The first cycle will be 35 days long (from day -7 through day 27) and the rest of the cycles will be 28 days long (from day 0 through day 27). Ganitumab will be given in an IV (a small plastic catheter put into a vein in your arm) in the clinic once every 2 weeks, starting on day 0.

There will be two phases to the study: Phase I and Phase II. In the Phase I portion of the study, the highest safe dose of dasatinib will be tested when given with ganitumab. Between 3 and 6 people will receive dasatinib at the first dose level, dasatinib once per day. If the side effects are acceptable, the next group of 3 to 6 people will receive the dose of dasatinib twice per day (dose level 2). If dose level 2 does not have unacceptable side effects, this will be the dose that will be used in the Phase II portion of the study

If unacceptable side effects are seen at the first dose level, additional patients will receive a lower dose of dasatinib (dose level -1) to make sure we find the maximum dose that is tolerated. If you are a patient enrolled early in this study you may receive a lower dose than those who are enrolled later.

In the Phase II portion of the study, up to an additional 10 people will be given the highest safe dose of dasatinib tested and the same dose of ganitumab as was given in Phase I.

Everyone will take dasatinib with at least 8 ounces of water, with or without food. Tablets should be swallowed whole; do not break or chew the tablets. If the dasatinib causes stomach upset, you should take it with a light meal. If you vomit within 30 minutes of swallowing the tablet(s), you can repeat the dose. But if you vomit later than 30 minutes after taking the dose, do not repeat it. Wait until the next day to take your next dose. We ask that you keep a medication diary to record when you get the study medication at home, and any symptoms that you may have as a result of the study medication, including how you treat the symptoms. Complete this medication diary every day and bring it to clinic with you when you come. Also bring the medication bottle and any remaining tablets to each clinic visit. If tablets are accidentally crushed or broken, caregivers should wear disposable chemotherapy gloves, which will be provided. Pregnant women should avoid exposure to crushed and/or broken tablets.

Because the dasatinib has the potential to interact with other medications and some foods, you will be given a drug interaction handout and wallet card as a resource for yourself, caregivers

and other health care providers. Do not take any new medications, even over the counter medications, without first talking to your study doctor.

Because some antacids may affect the way your body absorbs dasatinib, you should only take certain types of them (such as Maalox®, or Mylanta®). Please discuss this with your study doctor before beginning to take them. When taking the antacid your study doctor prescribes, do NOT take them within 2 hours before or 2 hours after your dasatinib dose.

Substances that affect your blood's ability to form clots, such as aspirin, nonsteroidal anti-inflammatory drugs (like motrin, ibuprofen), some antibiotics, some cardiovascular and lipid-lowering drugs, and some antidepressants should be avoided. It is important that you discuss any new drugs (prescription or over the counter) with your study doctor before starting.

Avoid drinking grapefruit juice or eating grapefruit until the study is over. You should not take St. John's wort while you are taking dasatinib.

You will come to the POB clinic every two weeks and be given the ganitumab in an IV. The first infusion will be given to you over about 1 hour. If you tolerate the first infusion, the second and subsequent infusions can be given over about 30 minutes. Let your study staff know if you experience any unusual feelings during the infusion (such as chills, difficulty breathing, headache or dizziness), because the infusion can be slowed or temporarily stopped to reduce these effects.

HOW LONG WILL I BE IN THIS STUDY?

You will take the dasatinib every day for 35 days during the first cycle, and for 28 days in subsequent cycles. You will be given the ganitumab once every 2 weeks. You can continue to take dasatinib-ganitumab as long as you do not have unacceptable toxicities or your tumor(s) do not get worse. If you have side effects the dose of dasatinib and/or ganitumab may be held for a short time and the dose(s) may be reduced to prevent return of the side effect. Two dose reductions for dasatinib and one dose reduction for ganitumab are allowed on this study. If the side effect(s) is too severe, or side effect(s) recur after the dose reductions, dasatinib-ganitumab may need to be stopped.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests and procedures that you will need to have if you take part in this study.

Before you begin the study:

You will need to have the following extra tests to find out if you can be in the study:

- Pregnancy test (if you are a woman who could have children)
- EKG (electrocardiogram), a test that checks the electrical activity of your heart
- Echocardiogram (a sonogram [uses sounds waves] of the heart that allows us to identify any problems with the heart valves or muscle movement.)
- Optional biopsy of tumor. This will be further discussed later in the consent.

During the study:

- EKG will be done before each cycle.
- Echocardiogram will be performed prior to cycles 1 and 2, and then before each scan to evaluate your tumor(s), (i.e. before cycles 3, 5, 7), and repeated more frequently if your doctor thinks it is needed.
- Pregnancy test will be performed before starting treatment and then before each scan to evaluate your tumor(s), (i.e. before cycles 3, 5, 7), if you are a female who can get pregnant.

- Tissue studies (tissue obtained during a previous surgery or biopsy): everyone participating will have tissue requested to study the changes in cell activities of patients with ERMS and ARMS. Your name will not be attached to your tissue; it will be identified using a study number. Only the investigator and research team will have access to the information that links your personal information to your tissue sample.

At the end of treatment with dasatinib-ganitumab you will have an evaluation at the NIH. At this visit you will have a physical exam, blood and urine tests and scans/x-rays to measure your tumor.

A STUDY CALENDAR THAT SHOWS HOW OFTEN THESE TESTS AND PROCEDURES WILL BE DONE IS ATTACHED.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

If you choose to take part in this study, there is a risk that ganitumab (AMG 479) and dasatinib may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions which you normally do not discuss
- May not be able to take part in future studies

The ganitumab (AMG 479) and dasatinib used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important points about how you and the study doctor can make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

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

Risks of Dasatinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving dasatinib, more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea • Tiredness • Bruising, bleeding • Pain • Headache • Shortness of breath • Fluid in the body • Rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving dasatinib, from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Bloating, constipation, heartburn, vomiting • Bleeding from multiple sites • Internal bleeding which may cause black tarry stool or blood in vomit • Sores in the mouth which may cause difficulty swallowing • Swelling of the body • Fever • Weight gain • Weight loss, loss of appetite • Dizziness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving dasatinib, from 4 to 20 may have:
• Cough, sore throat • Damage to organs (lungs, brain, others) which may cause shortness of breath, changes in thinking • Hair loss, itching, acne • Flushing

RARE, AND SERIOUS In 100 people receiving dasatinib, 3 or fewer may have:
• Heart failure, heart attack which may cause shortness of breath, swelling of ankles, and tiredness • Change in the heart rhythm • Kidney damage which may require dialysis • Bone growth may stop early in teenagers leading to short stature • Loss of bone tissue • Decreased height in children and adolescents • Enlarged breasts in males • Bleeding in the brain which may cause confusion • Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Inflammation of the lungs which can cause shortness of breath and difficulty breathing

Risks of Ganitumab

COMMON, SOME MAY BE SERIOUS In 100 people receiving Ganitumab (AMG 479), more than 20 and up to 100 may have:
• Tiredness • Reaction during or following a drug infusion which may cause fever, chills, low blood pressure

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Ganitumab (AMG 479), from 4 to 20 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Bruising, bleeding • Infection, especially when white blood cell count is low • Loss of appetite • Pain in muscles • Rash

RARE, AND SERIOUS In 100 people receiving Ganitumab (AMG 479), 3 or fewer may have:
• Hearing loss • Ganitumab may cause damage to the lung that may cause shortness of breath when receiving radiotherapy to the lungs shortly before or after treatment with ganitumab.

Reproductive Risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Both male and female participants must use effective birth control measures while participating in this study and for at least 4 months after the last dose of dasatinib-ganitumab. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Optional birth control methods include, but are not limited to, abstinence, oral birth control pills, an IUD, or condoms with spermicide. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately. A patient who becomes pregnant while on study will immediately be taken off study.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

Treatment with dasatinib-ganitumab may cause your tumor(s) to stop growing or shrink or it may lessen the symptoms, such as pain, that are caused by the tumor. However, because there is not much information about the combination of the drugs' effects on your type of tumor, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may benefit others. Your samples may be helpful to research. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization helping the investigators to run the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

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.

ADDITIONAL STUDIES SECTION

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

TUMOR BIOPSY

Biopsy of your tumor (optional): a biopsy of your tumor (take a small piece of your tumor tissue using a large needle) will be done before you start the study drugs, sometime during the first week of treatment and again if your tumor(s) begin to enlarge. This biopsy will only be requested if you are 12 years old or older, and provided the biopsy can be obtained safely, and are willing to participate in our companion protocol 10-C-0086. This tumor biopsy is optional. With this biopsy tissue we will study the changes that these study agents cause in the tumor of people with ERMS and ARMS. You can agree now to allow us to biopsy your tumor and change your mind later. This tissue will also undergo genomic analysis at a laboratory called NantOmics. Your name will not be attached to your tissue; it will be identified using a study number. Only the

investigator and research team will have access to the information that links your personal information to your tissue sample.

What is involved?

A doctor will use a hollow needle attached to a syringe to enter a tumor, then withdraw (aspirate) a small amount of tissue from the tumor. The doctor may use a scan or ultrasound to guide the needle directly to the tumor. Depending upon the location of the tumor, the doctor may use numbing medicine (called local anesthetic) to numb the area before the biopsy.

What are the possible risks?

The risks will be explained to you fully in a different consent. In general, the risks include bleeding, pain, scarring and infection. If there is bleeding under the skin, a hematoma or collection of blood at the biopsy site may occur. Other risks depend on the location of the tumor being sampled. The doctor will discuss these specific risks with you before the procedure.

How will information about me be kept private?

Your tumor samples will be identified and stored using a number and not your name. Only the study investigator and research team taking care of you on this study will have access to your name.

What are the possible benefits?

The use of your biopsy specimens will be for research purposes only and will not benefit you. Results of research done on your tumor specimens will not be available to you or your doctor, but it will help us better understand how this study drug works on tumors, and it might help people who have these types of tumors in the future.

Are there any costs or payments?

There are no costs to you. You will not be paid for your tissue. The cost of biopsy, storage and testing will be paid by the study investigators or collaborators in this study.

What if I change my mind?

If you decide now that you will undergo the biopsy, you can change your mind at any time. Just let us know at the time of the biopsy or contact us (office of Dr. Heske, Principal Investigator: 240-760-6197) and let us know that you do not want to have the biopsy.

What if I have more questions?

If you have additional questions, please contact the office of Dr. Heske, Principal Investigator: 240-760-6197.

Please circle your answer: I choose to take part in the tumor biopsy:

YES NO

BLOOD AND TISSUE STORAGE

What is involved?

Should any leftover blood remain after completing the studies described in earlier sections, we would like to keep the remaining blood for future research.

What are the possible risks?

There are no known risks as your blood and tissue samples have already been collected. No additional procedures will be performed.

How will information about me be kept private?

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. The remaining specimens and your data will be identified by a number only. Only the study investigator and research team taking care of you on this study will have access to your name.

What are the possible benefits?

The use of your specimens and data will be 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 these types of tumors and other diseases in the future.

Are there any costs or payments?

There are no costs to you. You will not be paid for your tissue or data. The cost of storage and testing will be paid by the study investigators or collaborators in this study.

What if I change my mind?

If you decide now that your specimens and data can be kept for research, you can change your mind at any time. Just contact us (office of Dr. Heske, Principal Investigator: 240-760-6197) and let us know that you do not want us to use your specimens and/or data. Then any specimens that remain will be destroyed, and your data will not be used for future research.

What if I have more questions?

If you have additional questions, please contact the office of Dr. Heske, Principal Investigator: 240-760-6197.

Please circle your answer: My specimens and data may be used for future research:

YES NO

STUDY CALENDAR

Test/Procedure	Pre-treatment	During Cycle 1	During Cycles 2 through end of treatment	Completion/ Stopping treatment
Medical history, Physical exam, vital signs	X	Weekly starting from day -7	On days 0 and 14	X
Standard blood tests	X	Weekly starting from day -7	Weekly for cycles 2 and 3, then every other week thereafter	X
Urine test	X	Weekly starting from day -7	Prior to each subsequent cycle	X
EKG	X		Prior to each subsequent cycle	
Echocardiogram	X		At the start of cycles 1,2, 3, 5, 7, 9, 11 etc.	
Dasatinib, swallow tablets(s); record in the diary		Days -7 through Day 28	Day 0 through Day 28	
Ganitumab, IV every 2 weeks		Day 0 and Day 14	Day 0 and Day 14	
Tumor biopsy (optional if you are 12 years of age or older)	X	During week 1		If your tumor(s) grow
Pregnancy test	X		Prior to cycle 3, 5, 7, 9, 11, etc	
Tumor evaluations	X		Prior to cycle 3, 5, 7, 9, 11, etc	

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

The NCI generally does not cover expenses during screening. If you are scheduled for and begin treatment, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- 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.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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 NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study sponsor and any drug company supporting the study.

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.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you may be responsible for any costs.

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, Christine Heske, MD, Christine.heske@nih.gov, 240-760-6197. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Parent/Guardian of a Minor Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I give permission for my child to take part in this study.

Signature of Parent/Guardian	Print Name of Parent/Guardian	Date
Signature of Parent/Guardian *(as applicable)*	Print Name of Parent/Guardian	Date

Assent: *(Use this section only when this process is approved by an IRB for older minors. Do not use if an IRB requires a separate assent form for this population.)*

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

Assent of Minor: *(as applicable)*

Signature of Minor	Print Name of Minor	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral

short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.

NOTES FOR LOCAL INVESTIGATORS*:

- The goal of the informed consent process is to provide people with sufficient information for making informed choices about participating in research. The consent form provides a summary of the study, of the individual's rights as a study participant, and documents their willingness to participate. The consent form is, however, only one piece of an ongoing exchange of information between the investigator and study participant. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/

- A blank line, "_____", indicates that the local investigator should provide the appropriate information before submitting to the IRB.

*These notes for investigators are instructional and should not be included in the consent form sent to IRBs.

Consent Form

Study Title for Study Participants: Das-Ganit in Rhabdomyosarcoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10003: A Phase I/II Trial of the Insulin-like Growth Factor 1 Receptor (IGF-1R) Antibody AMG479 (Ganitumab) in Combination with the Src Family Kinase (SFK) Inhibitor Dasatinib in Patients with Embryonal and Alveolar Rhabdomyosarcoma

What is the usual approach to my diagnosis?

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma of childhood. Two major types of RMS are embryonal rhabdomyosarcoma (ERMS) and alveolar rhabdomyosarcoma (ARMS). The treatments for RMS include surgery, radiation therapy or chemotherapy. Some of the agents used to treat rhabdomyosarcoma are approved by the U.S. Food and Drug Administration (FDA) for other indications. New types of treatments being tested in clinical trials include high-dose chemotherapy with stem cell transplant, immunotherapy, or targeted therapy.

The insulin-like growth factor (IGF) system plays an important role in many cancers. Over-expression of the type 1 IGF receptor (IGF-1R) has been observed in sarcoma. An enzyme called YES is also highly expressed in both ERMS and ARMS. Treatment blocking both IGF and YES appears to slow tumor growth of ERMS and ARMS cells studied in the laboratory.

Dasatinib is an enzyme inhibitor that may block over-expression of YES. Dasatinib also appears to have anticancer activity in some cancers. Ganitumab is a monoclonal antibody directed specifically against IGF-1R to suppress tumor growth.

What is the usual approach to my cancer?

You are being asked to participate in this trial because you have ERMS or ARMS and the other known treatments for your disorder, such as surgery, radiation therapy or chemotherapy, have not proven effective for you. People who are not in a study are usually treated with surgical removal of their tumor, radiation, and/or chemotherapy. You may decide not to receive any treatment directed at shrinking your tumor(s) at this point in time.

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

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

Please talk to your doctor about these and other options.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you are not able to meet the study requirements for taking selumetinib or keep your appointments
- If the study is stopped by the sponsor, IRB or FDA. Even though it probably won't happen, it is possible that the manufacturer may not continue to provide the selumetinib to the NCI for some reason. If this would occur, the study will be closed and your study doctor will talk to you about other treatment options (including continuing selumetinib if it becomes commercially available).

Why is this study being done?

The purposes of this research study are:

1. To find the safe dose of dasatinib when given with ganitumab in patients with ERMS and ARMS.
2. To assess if the combination of ganitumab and dasatinib is helpful in the treatment of your type of tumor(s) (causes your tumor to shrink or slow down the growth), or can increase survival.
3. To study the side effects of the combination of ganitumab and dasatinib.
4. To study how ganitumab and dasatinib act on the tumors of people with RMS.
5. To do genomic analysis of tissue samples of patients with ERMS and ARMS (you will be asked to participate in another study for this called protocol 10-C-0086: *Comprehensive Omics Analysis of Pediatric Solid Tumors and Establishment of a Repository for Related Biological Studies)*

Ganitumab is being used in clinical studies and has been given to adults and children with different types of tumors. Dasatinib was approved by the U.S. Food and Drug Administration (FDA) for treatment of adults with a type of chronic myeloid leukemia (CML). Ganitumab has not been approved by the U.S. Food and Drug Administration (FDA) for any indication. Ganitumab and the combination of ganitumab and dasatinib are experimental, meaning they have not been approved by the FDA, but are approved for use in this clinical trial.

Up to 24 evaluable patients may take part in this study.

What are the study groups?

All study participants will get the same study intervention. You will take the dasatinib pills by mouth every day. The treatment will be divided into cycles. The first cycle will be 35 days long (from day -7 through day 27) and the rest of the cycles will be 28 days long (from day 0 through day 27). Ganitumab will be given in an IV (a small plastic catheter put into a vein in your arm) in the clinic once every 2 weeks, starting on day 0.

There will be two phases to the study: Phase I and Phase II. In the Phase I portion of the study, the highest safe dose of dasatinib will be tested when given with ganitumab. Between 3 and 6 people will receive dasatinib at the first dose level, dasatinib once per day. If the side effects are acceptable, the next group of 3 to 6 people will receive the dose of dasatinib twice per day (dose level 2). If dose level 2 does not have unacceptable side effects, this will be the dose that will be used in the Phase II portion of the study

If unacceptable side effects are seen at the first dose level, additional patients will receive a lower dose of dasatinib (dose level -1) to make sure we find the maximum dose that is tolerated. If you are a patient enrolled early in this study you may receive a lower dose than those who are enrolled later.

In the Phase II portion of the study, up to an additional 10 people will be given the highest safe dose of dasatinib tested and the same dose of ganitumab as was given in Phase I.

Everyone will take dasatinib with at least 8 ounces of water, with or without food. Tablets should be swallowed whole; do not break or chew the tablets. If the dasatinib causes stomach upset, you should take it with a light meal. If you vomit within 30 minutes of swallowing the tablet(s), you can repeat the dose. But if you vomit later than 30 minutes after taking the dose, do not repeat it. Wait until the next day to take your next dose. We ask that you keep a

medication diary to record when you get the study medication at home, and any symptoms that you may have as a result of the study medication, including how you treat the symptoms. Complete this medication diary every day and bring it to clinic with you when you come. Also bring the medication bottle and any remaining tablets to each clinic visit. If tablets are accidentally crushed or broken, caregivers should wear disposable chemotherapy gloves, which will be provided. Pregnant women should avoid exposure to crushed and/or broken tablets.

Because the dasatinib has the potential to interact with other medications and some foods, you will be given a drug interaction handout and wallet card as a resource for yourself, caregivers and other health care providers. Do not take any new medications, even over the counter medications, without first talking to your study doctor.

Because some antacids may affect the way your body absorbs dasatinib, you should only take certain types of them (such as Maalox®, or Mylanta®). Please discuss this with your study doctor before beginning to take them. When taking the antacid your study doctor prescribes, do NOT take them within 2 hours before or 2 hours after your dasatinib dose.

Substances that affect your blood's ability to form clots, such as aspirin, nonsteroidal anti-inflammatory drugs (like motrin, ibuprofen), some antibiotics, some cardiovascular and lipid-lowering drugs, and some antidepressants should be avoided. It is important that you discuss any new drugs (prescription or over the counter) with your study doctor before starting.

Avoid drinking grapefruit juice or eating grapefruit until the study is over. You should not take St. John's wort while you are taking dasatinib.

You will come to the clinic every two weeks and be given the ganitumab in an IV. The first infusion will be given to you over about 1 hour. If you tolerate the first infusion, the second and subsequent infusions can be given over about 30 minutes. Let your study staff know if you experience any unusual feelings during the infusion (such as chills, difficulty breathing, headache or dizziness), because the infusion can be slowed or temporarily stopped to reduce these effects.

How Long Will I Be in This Study?

You will take the dasatinib every day for 35 days during the first cycle, and for 28 days in subsequent cycles. You will be given the ganitumab once every 2 weeks. You can continue to take dasatinib-ganitumab as long as you do not have unacceptable toxicities or your tumor(s) do not get worse. If you have side effects the dose of dasatinib and/or ganitumab may be held for a short time and the dose(s) may be reduced to prevent return of the side effect. Two dose reductions for dasatinib and one dose reduction for ganitumab are allowed on this study. If the side effect(s) is too severe, or side effect(s) recur after the dose reductions, dasatinib-ganitumab may need to be stopped.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests and procedures that you will need to have if you take part in this study.

Before you begin the study:

You will need to have the following extra tests to find out if you can be in the study:

- Pregnancy test (if you are a woman who could have children)
- EKG (electrocardiogram), a test that checks the electrical activity of your heart
- Echocardiogram (a sonogram [uses sounds waves] of the heart that allows us to identify any problems with the heart valves or muscle movement.)
- Optional biopsy of tumor. This will be further discussed later in the consent.

During the study:

- EKG will be done before each cycle.
- Echocardiogram will be performed prior to cycles 1 and 2, and then before each scan to evaluate your tumor(s), (i.e. before cycles 3, 5, 7), and repeated more frequently if your doctor thinks it is needed.
- Pregnancy test will be performed before starting treatment and then before each scan to evaluate your tumor(s), (i.e. before cycles 3, 5, 7), if you are a female who can get pregnant.
- Tissue studies (tissue obtained during a previous surgery or biopsy): everyone participating will have tissue requested to study the changes in cell activities of patients with ERMS and ARMS. Your name will not be attached to your tissue; it will be identified using a study number. Only the investigator and research team will have access to the information that links your personal information to your tissue sample.

At the end of treatment with dasatinib-ganitumab you will have an evaluation at _____. At this visit you will have a physical exam, blood and urine tests and scans/x-rays to measure your tumor.

A study calendar that shows how often these tests and procedures will be done is attached.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that ganitumab (AMG 479) and dasatinib may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions which you normally do not discuss
- May not be able to take part in future studies

The ganitumab (AMG479) and dasatinib used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.

- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important points about how you and the study doctor can make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

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

Risks of Dasatinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving dasatinib, more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea • Tiredness • Bruising, bleeding • Pain • Headache • Shortness of breath • Fluid in the body • Rash

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

- Infection, especially when white blood cell count is low
- Bloating, constipation, heartburn, vomiting
- Bleeding from multiple sites
- Internal bleeding which may cause black tarry stool or blood in vomit
- Sores in the mouth which may cause difficulty swallowing
- Swelling of the body
- Fever
- Weight gain
- Weight loss, loss of appetite
- Dizziness
- Cough, sore throat
- Damage to organs (lungs, brain, others) which may cause shortness of breath, changes in thinking
- Hair loss, itching, acne
- Flushing

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

- Heart failure, heart attack which may cause shortness of breath, swelling of ankles, and tiredness
- Change in the heart rhythm
- Kidney damage which may require dialysis
- Bone growth may stop early in teenagers leading to short stature
- Loss of bone tissue
- Decreased height in children and adolescents
- Enlarged breasts in males
- Bleeding in the brain which may cause confusion
- Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body
- Inflammation of the lungs which can cause shortness of breath and difficulty breathing

Risks of Ganitumab

COMMON, SOME MAY BE SERIOUS In 100 people receiving Ganitumab (AMG 479), more than 20 and up to 100 may have:
• Tiredness • Reaction during or following a drug infusion which may cause fever, chills, low blood pressure

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Ganitumab (AMG 479), from 4 to 20 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Bruising, bleeding • Infection, especially when white blood cell count is low • Loss of appetite • Pain in muscles • Rash

RARE, AND SERIOUS In 100 people receiving Ganitumab (AMG 479), 3 or fewer may have:
• Hearing loss • Ganitumab may cause damage to the lung that may cause shortness of breath when receiving radiotherapy to the lungs shortly before or after treatment with ganitumab.

Reproductive Risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Both male and female participants must use effective birth control measures while participating in this study and for at least 4 months after the last dose of dasatinib-ganitumab. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Optional birth control methods include, but are not limited to, abstinence, oral birth control pills, an IUD, or condoms with spermicide. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately. A patient who becomes pregnant while on study will immediately be taken off study.

What possible benefits can I expect from taking part in this study?

Treatment with dasatinib-ganitumab may cause your tumor(s) to stop growing or shrink or it may lessen the symptoms, such as pain, that are caused by the tumor. However, because there is not much information about the combination of the drugs' effects on your type of tumor, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may benefit others. Your samples may be helpful to research. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization helping the investigators to run the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules

If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

Study treatment will be supplied at no charge while you take part in this study. You and/or your health plan/insurance company will need to pay for all of the other costs of treating your tumors while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

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

(Note to consent form authors and investigators: Insert a description of any compensation for participation or reimbursement for expenses.)

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

The NCI has recommended that HIPAA regulations be addressed by the local institution. Language pertaining to HIPAA compliance may or may not be included in the local consent form, depending on local institutional policy.

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Qualified representatives from the pharmaceutical collaborator, maker of selumetinib.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- Representatives of the National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in overseeing research

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION

This section is about optional studies you can choose to take part in

Biopsy of your tumor (optional): a biopsy of your tumor (take a small piece of your tumor tissue using a large needle) will be done before you start the study drugs, sometime during the first week of treatment and again if your tumor(s) begin to enlarge. This biopsy will only be requested if you are 12 years old or older, and provided the biopsy can be obtained safely, and are willing to participate in our companion protocol 10-C-0086. This tumor biopsy is optional. With this biopsy tissue we will study the changes that these study agents cause in the tumor of people with ERMS and ARMS. You can agree now to allow us to biopsy your tumor and change your mind later. This tissue will also undergo genomic analysis at a laboratory called NantOmics. Your name will not be attached to your tissue; it will be identified using a study number. Only the investigator and research team will have access to the information that links your personal information to your tissue sample.

What is involved?

A doctor will use a hollow needle attached to a syringe to enter a tumor, then withdraw (aspirate) a small amount of tissue from the tumor. The doctor may use a scan or ultrasound to guide the needle directly to the tumor. Depending upon the location of the tumor, the doctor may use numbing medicine (called local anesthetic) to numb the area before the biopsy.

What are the possible risks?

The risks will be explained to you fully in a different consent. In general, the risks include bleeding, pain, scarring and infection. If there is bleeding under the skin, a hematoma or collection of blood at the biopsy site may occur. Other risks depend on the location of the tumor being sampled. The doctor will discuss these specific risks with you before the procedure.

How will information about me be kept private?

Your tumor samples will be identified and stored using a number and not your name. Only the study investigator and research team taking care of you on this study will have access to your name.

What are the possible benefits?

The use of your biopsy specimens will be for research purposes only and will not benefit you. Results of research done on your tumor specimens will not be available to you or your doctor, but it will help us better understand how this study drug works on tumors, and it might help people who have these types of tumors in the future.

Are there any costs or payments?

There are no costs to you. You will not be paid for your tissue. The cost of biopsy, storage and testing will be paid by the study investigators or collaborators in this study.

What if I change my mind?

If you decide now that you will undergo the biopsy, you can change your mind at any time. Just let us know at the time of the biopsy or contact us _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number)* and let us know that you do not want to have the biopsy.

What if I have more questions?

If you have additional questions, please contact the office of Dr. Heske, Principal Investigator: 240-760-6197.

Yes No NA Initials:_____ Date: _____

This is the end of the section about optional studies.

Blood and Tissue Storage

What is involved?

Should any leftover blood remain after completing the studies described in earlier sections, we would like to keep the remaining blood for future research.

What are the possible risks?

There are no known risks as your blood and tissue samples have already been collected. No additional procedures will be performed.

How will information about me be kept private?

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. The remaining specimens and your data will be identified by a number only. Only the study investigator and research team taking care of you on this study will have access to your name.

What are the possible benefits?

The use of your specimens and data will be 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 these types of tumors and other diseases in the future.

Are there any costs or payments?

There are no costs to you. You will not be paid for your tissue or data. The cost of storage and testing will be paid by the study investigators or collaborators in this study.

What if I change my mind?

If you decide now that your specimens and data can be kept for research, you can change your mind at any time. Just contact us (office of _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number)*) and let us know that you do not want us to use your specimens and/or data. Then any specimens that remain will be destroyed, and your data will not be used for future research.

What if I have more questions?

If you have additional questions, please contact the office of _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number)*.

Study Calendar

Test/Procedure	**Pre-treatment**	**During Cycle 1**	**During Cycles 2 through end of treatment**	**Completion/ Stopping treatment**
Medical history, Physical exam, vital signs	X	Weekly starting from day -7	On days 0 and 14	X
Standard blood tests	X	Weekly starting from day -7	Weekly for cycles 2 and 3, then every other week thereafter	X
Urine test	X	Weekly starting from day -7	Prior to each subsequent cycle	X
EKG	X		Prior to each subsequent cycle	
Echocardiogram	X		At the start of cycles 1,2, 3, 5, 7, 9, 11 etc.	
Dasatinib, swallow tablets(s); record in the diary		Days -7 through Day 28	Day 0 through Day 28	
Ganitumab, IV every 2 weeks		Day 0 and Day 14	Day 0 and Day 14	

Tumor biopsy (optional if you are 12 years of age or older)	X	During week 1		If your tumor(s) grow
Pregnancy test	X		Prior to cycle 3, 5, 7, 9, 11, etc	
Tumor evaluations	X		Prior to cycle 3, 5, 7, 9, 11, etc	

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____