NCI Protocol #: 10480
Local Protocol #: 2022-0246
Protocol Version Date: December 13, 2022

Protocol Title: Phase Ib/II Study of EPA-based EphA2 Targeted Therapy for Patients with Metastatic Triple-Negative Inflammatory Breast Cancer

Informed Consent Version Date: December 13, 2022

I. Summary of Changes:

#	Section	Comments
1.	General	Updated version date in the footer from April 27, 2022 to December 13, 2022. No change in the content of the informed consent. **PI response:** To be consistent with the updated protocol version date.

Research Study Informed Consent Document for Phase 1b Dose Escalation

Study Title for Participants: Testing an omega-3 fatty acid-based anti-cancer therapy for patients with inflammatory breast cancer that has spread to other parts of the body

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10480, "Phase Ib/II Study of EPA-based EphA2 Targeted Therapy for Patients with Metastatic Triple-Negative Inflammatory Breast Cancer,"(NCT#05198843)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have metastatic triple-negative inflammatory breast cancer (TN-IBC).

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

What is the highest dose of two drugs called dasatinib and icosapent ethyl (EPA) in combination that can be safely and tolerably taken by people with metastatic TN-IBC?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your metastatic TN-IBC. The usual approach is defined as care most people get for metastatic TN-IBC.

What is the usual approach to my metastatic TN-IBC?

The usual approach for patients who are not in a study is treatment with chemotherapy. There are several chemotherapy drugs approved by the Food and Drug Administration (FDA). There are no treatments that are proven to help patients with your health condition live longer.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get EPA and dasatanib until your disease gets worse or the side effects become too severe.

After you finish your study treatment, your doctor will continue to follow your condition for 3 months and watch you for side effects. They will check you 1 month after your last treatment dose or before you start a new treatment, whichever comes first, and 3 months after your last treatment dose. You can either visit the clinic for your 1-month and 3-month follow-up visits or contact your doctor by phone. Then they will check you by phone every 3 months for 2 years after treatment.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Anemia which may require blood transfusion
- Diarrhea, nausea
- Fluid in the body
- Bruising, bleeding
- Pain

There may be some risks that the study doctors do not yet know about.

Benefits

There is some evidence in animals, in living human cells and in living animal cells that this treatment can shrink or stabilize metastatic TN-IBC, but we do not know if this will happen in people. It is unlikely that the combination of EPA and dasatinib will help you live longer. This study may help the study doctors learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the safety of a drug called dasatinib in combination with EPA. Dasatinib has been tested in humans, but has not been tested in combination with EPA, also known as icosapent ethyl, in patients with metastatic TN-IBC. This study tests different doses of the drug to see which dose is safer for people. There will be about 18 people taking part in this study.

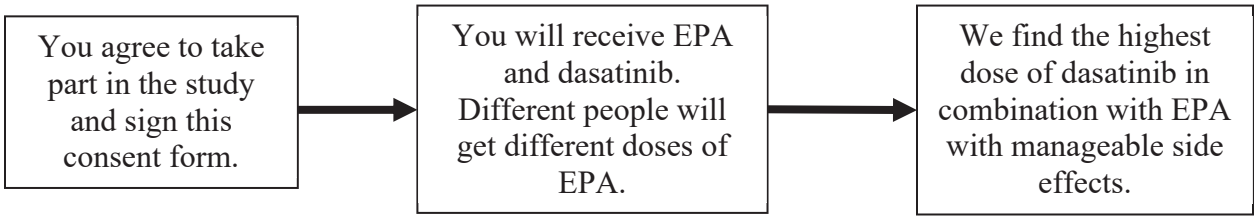
What are the study groups?

Different people taking part in this study will get different doses of the study drug EPA in combination with dasatinib. Treatment schedule: You will get dasatinib as a tablet you take by mouth once a day with or without food. You will get EPA as a capsule you take by mouth twice a day with food. Each cycle lasts 28 days. This study will continue until your disease gets worse or the side effects become too severe. See the study calendar for more information.

The first 3 people taking part in this study will get the lowest dose of EPA. If the drug combination does not cause serious side effects, the current dose group and the next group of people in the study will get a higher dose of EPA. We will repeat the above steps until the maximum sample size of 18 is reached. The study doctor will watch each group carefully as they increase the dose. The EPA dose will continue to increase for every new group until people have serious side effects that require the dose to be lower or have reached the highest EPA dose to be given. Once this dose is found, the study is stopped.

You will not be able to get additional doses of the drugs. These drugs are not approved by the FDA for treatment of your disease.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

You will need to have a mandatory biopsy and blood sample taken for the study before you begin study treatment and after Cycle 2. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. The biopsies will be used to see if your cancer is responding to the combination of dasatinib and EPA. You and your study doctor will not get the results of this testing. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

A patient study calendar is attached at the end of this document. It shows how often these exams, tests, and procedures will be done.

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

General Risks

If you choose to take part in this study, there is a risk that the study drug may not be as good as the usual approach for your cancer 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 about things you normally do not discuss.
- May not be able to take part in future studies.

The study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 3 months after you have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Refer to the section under "Optional studies" for procedures followed if there is any leftover specimen that may possibly be stored for biobanking.

Side Effect Risks

The drugs 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 let you know if changes occur that may affect your health.

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

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. 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 ways to 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.

You should notify your doctor immediately at the first sign of poorly formed or loose stools or an increased frequency of bowel movements. Loperamide (Imodium) should be kept on hand and should be taken as recommended by your doctor. This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that 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.

Possible Side Effects of Dasatinib (BMS-354825, Sprycel)
(Table Version Date: September 10, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving dasatinib (BMS-354825, Sprycel), 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 (BMS-354825, Sprycel), 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 (BMS-354825, Sprycel), 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

Possible Side Effects of Icosapent ethyl (EPA)

RARE, AND MILD In 100 people receiving EPA (Vascepa), 3 or fewer may have:
• Joint pain • Pain in muscles, bones, tendons, and nerves • Swelling of lower legs or hands • Constipation • Swelling, redness and tenderness in joints • Heart palpitations, shortness of breath, and fatigue • Sore throat, difficulty swallowing

Additional Drug Risks

The study drug could interact with other drugs, including antacids and blood thinners. These drugs may increase your side effects, reduce the amounts of study drugs in your body, and lower the effectiveness of the study treatment.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study

    - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 3 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the dasatinib and EPA ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The biopsy for testing tumor response at the beginning of the study and after Cycle 2.
- The blood collection for testing tumor response at the beginning of the study and after Cycle 2.

You or your insurance provider will not have to pay for the dasatinib or EPA while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The Texas Experimental Cancer Therapeutic Network (TEX-CTN) which includes 4 sites: The University of Texas (UT) MD Anderson Cancer Center (Houston, TX), UT Health San Antonio MD Anderson Cancer Center, UT Medical Branch (UTMB) at Galveston, and UT Austin.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now 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).

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.

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, and email address if appropriate*)

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies 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.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and

your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these 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.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, tissue and blood will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by Nationwide Children's Hospital in Columbus, Ohio and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood and/or tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- 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 samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For

example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. Any leftover tissue from the tissue that was collected at the time of your mandatory biopsy before you began study treatment and after completion of Cycle 2, and any leftover blood from the mandatory collections before you began study treatment, and after completion of Cycle 2, will be sent to the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance.

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor,(*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the 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 and dated copy of this form. I agree to take part in the main study.

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Patient Study Calendar

	Before you begin the study	Cycle 1				Cycle 2				Cycle 3+				Off Study[a]
		Wk 1	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4	Wk 9	Wk 10	Wk 11	Wk 12	
Dasatinib[b]		X	X	X	X	X	X	X	X	X	X	X	X	
Icosapent ethyl (EPA)[b]		X	X	X	X	X	X	X	X	X	X	X	X	
Pre-study [Before you begin study treatment] procedures including informed consent, demographics, height and medical history	X													
Review of all medications that you are taking	X	X----------X												
Physical exam, vital signs and weight	X	X				X				X				X
Assessment of how you perform everyday tasks and activities	X													
Blood draws for complete blood count and general health status	X	X				X				X				X
EKG (as indicated by your doctor)	X													
Side effect evaluation		X----------X												
Medical imaging scans for tumor measurements	X	Tumor measurements are repeated every 8 weeks.												X
Blood or urine collection for pregnancy test [c]	X													
Mandatory Biopsy for research	X								X					
Mandatory Blood collection for research	X								X					

a: Off-study evaluations within 1 month after and 3 months after final study treatment.
b: Dose as assigned
c: Pregnancy test for women of childbearing potential.