

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

STUDY NUMBER: 14-C-0007 PRINCIPAL INVESTIGATOR: Geraldine O'Sullivan Coyne, MD, PhD

STUDY TITLE: Phase II Trial of the γ -secretase Inhibitor PF-03084014 in Adults with Desmoid Tumors/Aggressive Fibromatosis

Continuing Review Approved by the IRB on 03/12/19
 Amendment Approved by the IRB on 05/17/19 (K) Date posted to web: 05/31/19

Standard

INTRODUCTION

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

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

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

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

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

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

Why is this study being done?

The purpose of this study is to find out what effects, good and/or bad, the drug PF-03084014 may have on you and your tumor. Use of PF-03084014 is experimental. This study will measure whether taking this drug every day makes your tumors smaller. PF-03084014 has been tested in animals and is in the early stages of being tested in patients with different types of cancer. In an earlier clinical trial, some patients with desmoid tumors who took PF-03084014 for several months had their tumors become smaller.

This study may also help us find out whether your tumor has a variation in one of several genes that allow your tumor cells to form and grow. Blood, tissue, and tumor cells contain genes

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which are made up of DNA and which serve as the “instruction book” for each cell in the body. We know that variations in the genes in desmoid tumors are important for their growth. Identifying these tumor variations is one way scientists are trying to study and treat desmoids and other types of tumors.

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

You are being asked to take part in this research study because you have desmoid tumors that have progressed after receiving at least one line of standard treatment. People with desmoid tumors who are not in a study are usually treated with chemotherapy that has already been approved by the FDA, or surgery, or radiation therapy.

How many people will take part in this study?

About 17 people with desmoids will take part in this study.

Description of Research Study

To take part in this study, you must be willing to provide a tumor block (or slides taken from your tumor block) and one blood sample so that we can look for variations in the genes that allow your desmoids to form and grow. Your study doctor will explain these genetic research studies to you in more detail. **However, these studies may also reveal information about your hereditary risk of developing other diseases or serious illness that, if revealed, might affect your privacy. This is very important.** In order to protect your privacy, all samples collected on this study will be assigned a special unique code to protect your confidentiality. If you agree to allow us to save certain medical information for our research, your information would be kept in a secure computer database and “linked” with the unique code assigned to your samples. To further help protect your privacy, your medical information would be “unlinked” before we perform detailed genetic analysis of your samples so that we cannot connect the results back to you. The results of the research studies would not be reported to you, your family, or your doctor.

The total amount of blood collected at the beginning of the study is about 2 teaspoons.

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

During the study, you will take PF-03084014 by mouth twice a day every day. The study team will give you a diary to write down what time you take the drug each day as well as any side effects you may have. The team will also give you a chart describing the tests and procedures that will be done each day during the study.

Study tests, and procedures:

- CT scans to measure how your tumors are responding to PF-03084014 treatment will be done before you begin the study and then every 6 cycles (about every 4 months)

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- MRI scans are no longer mandatory and may be performed at the PI's discretion prior to start of study treatment, at the end of cycle 1, and then every 6 cycles (about every 4 months) to measure your tumors
- You will be asked to complete health-related quality of life and symptom questionnaires at each Clinical Center visit so that we can learn about symptoms from your disease, treatment-related symptoms commonly experienced by patients, and how these symptoms affect how you feel and are able to function. Filling in these questionnaires will take about 10 minutes each time.

Most of the exams, tests, and procedures you will have are part of your regular care such as a complete medical history, blood tests, and scans to measure your tumors. We would also do a pregnancy test in women who are able to become pregnant.

If you choose to take part in this study, then we will also ask you to consider some optional extra tests and procedures. **None** of these tests are part of the usual approach for desmoid tumors: these tests are being done for research to help us learn more about desmoids. If you choose not to have these optional research tests you will still receive study drug and have other tests that are part of the study.

- If you agree, we would also like to collect tumor biopsy samples before PF-03084014 is given and again after you have been taking the drug for several weeks. We would also like to collect some of your medical information (without personal identifiers), such as what type of tumor you have, what drugs you have taken, and whether or not your tumor responded to these drugs, but not your name or any other personally identifiable information.

How long will I be in this study?

If you are accepted and you choose to take part in this study, you will begin taking PF-03084014 by mouth twice a day. PF-03084014 is given in cycles; each cycle is 21 days (3 weeks) long. All of the people taking part in this study will initially be given the same dose of drug; this dose may be changed by your study doctor based on any side effects that you may experience. You will stay in the study as long as you are tolerating the drug and your tumors are either stable or getting better, but you can choose to leave the study at any time.

Birth Control

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you

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will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 6 months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

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

Risks or Discomforts of Participation

If you choose to take part in this study, there is a risk that you may:

- Lose time at work or home and spend more time in the hospital or doctor's office than usual
- Be asked sensitive or private questions which you normally do not discuss

The drug given in this study may affect how different parts of your body work, such as your liver, kidneys, heart, and blood. Your study doctor will be testing your blood and will let you know if changes occur that may affect your health. There is a risk that you could have side effects.

Here are important points about side effects:

- Your 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 serious and may even result in death.

Here are important points about how you and your study doctor can make side effects less of a problem:

- Tell your study doctor or medical team if you notice or feel anything different so that the team can see if you are having a side effect.
- Your study doctor may be able to treat some side effects.
- Your study doctor may change the dose of the study drug to try to reduce side effects.

The table below shows the most common and the most serious side effects of PF-03084014 that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible side effects of PF-03084014

- Diarrhea
- Vomiting
- Nausea
- Fatigue or tiredness
- Cough
- Rash
- Decreased appetite
- High levels of glucose in your blood (hyperglycemia)
- Low number of lymphocytes (cells involved with the immune system) in your blood (lymphocytopenia)
- Low number of platelets (cells that help blood clot) in your blood (thrombocytopenia)
- High levels of alanine transaminase (an enzyme made by your liver) in your blood (ALT increased)
- Low levels of potassium in your blood (hypokalemia)
- Low levels of phosphorus in your blood (hypophosphatemia)
- Rapidly progressing, life-threatening allergic reaction (anaphylactic shock)

Because some of the adverse events seen in patients taking PF-03084014 included fewer cells that fight infection, please tell your study team immediately if you have any of the symptoms of a fever, sore throat, or other signs of an infection.

Let your study doctor know of any questions you have about possible side effects. You can ask your study doctor and medical team questions about side effects at any time.

Potential Risks Related to Blood Samples

Possible side effects from drawing the blood sample include mild pain, bleeding, bruising, and infection at the site of the needle insertion. Fainting or light-headedness can sometimes occur, but usually last only a few minutes.

Potential Risks Associated With Gene Sequencing

We will also be performing a full genetic analysis on the tumor samples and blood of patients on this study. This analysis is investigational, and not approved or cleared by the FDA, and is for research purposes only. We will only do this analysis once we have deleted all information that identifies the sample as belonging to you before we perform this analysis. Deleting your

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information is important because by sequencing your tumor and blood cells for gene variations, we may find information about your hereditary risk of developing disease, such as an increased risk of cancer or other serious illness. Because you share some genetic information with your children, parents, brothers, sisters, and other blood relatives, this information may also tell us about your blood relatives' risk of developing disease. This information could affect your ability or the ability of your family to purchase long term care insurance, disability insurance, and life insurance. Your privacy is very important to us. The best way to protect your privacy is to delete your information from your samples before we do these research tests. This means that we will not be able to tell which patients' tumors have gene variations. We will not know if a given tumor with or without a variation is yours, and therefore will not be able to give you any information we learn. If you have any questions about this, please ask your study team.

While neither the public nor the controlled-access databases developed for this project will contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative).

There also may be other privacy risks that we have not foreseen.

There are state and federal laws that protect against genetic discrimination. There is a new federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

For more information, please visit

<http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfodoc.pdf>. A hard copy of the fact sheet can be provided to you on your request.

Potential Risks Related to Research-Related Imaging Studies

This research study involves exposure to radiation from up to 2 CT scans from biopsy collection. This radiation exposure is not required for your medical care and is for research purposes only.

The amount of radiation you will receive from up to 2 biopsy collections in this study is 1.6 rem. This dose is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, [An Introduction to Radiation for NIH Research Subjects](#).

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While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer. Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant you will not be permitted to give a tumor biopsy. It is best to avoid radiation exposure to unborn infants because they are more sensitive to radiation than adults.

Potential Benefits of Participation

Are there benefits to taking part in this study?

Taking part in this study may or may not make your health better. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the tumor. Because there is very little information about the effect of PF-03084014 on your tumor, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have desmoids.

Alternative Approaches or Treatments

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

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

- you may choose to have the usual approaches described above
- you may choose to take part in a different study, if one is available, such as chemotherapy or hormonal therapy or the investigational agents imatinib or sorafenib
- or you may choose not to be treated for desmoid, but you may want to receive comfort care to relieve symptoms

Please talk to your doctor about these and other options.

Research Subject's Rights

What are the costs of taking part in this study?

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

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done

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outside the Clinical Center, NIH if the study related treatment is not available at the NIH.

- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Will your medical information be kept private?

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.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The National Cancer Institute (NCI), which is sponsoring this study
- The drug company supplying PF-03084014 for the study
- The Institutional Review Board (IRB), a group of people who review the research with the goal of protecting the people who take part in the study
- The Food and Drug Administration (FDA), which regulates the testing of experimental drugs

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.

Stopping Therapy

You can decide to stop at any time. If you decide to stop for any reason, it is important to let your 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 include your medical information in the study. 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.

Your 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

MEDICAL RECORD**CONTINUATION SHEET for either:**

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

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

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- 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.

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

Optional Biopsy

Tumor biopsy: Only if you have disease that in the opinion of your study doctor can be biopsied safely, will we ask you to consider undergoing a procedure to collect tumor biopsy. If you agree, you will undergo imaging-directed biopsy of your tumor (removal of a small bit of tissue for research purposes) once before you receive the study drug PF-03084014 and again after you have been taking drug for about 5 months. After the first biopsy, if you decide not to have the second biopsy you will still receive study drug and have other tests that are part of the study.

You will be asked to sign a separate consent form for each biopsy procedure.

Biopsies will be done using a small bore needle under imaging guidance (CT, MRI, or ultrasound as deemed appropriate by the interventional radiologist performing the biopsy). Imaging helps the specialized radiologist know that the needle has been placed into the tumor mass. You will be counseled in more detail about the procedure and its risks at that time. Your safety is the most important thing at all times.

Even if you sign "yes" to have the biopsy, you can change your mind at any time. Please read the sentence below and think about your choice. After reading the sentence, circle and initial the answer that is right for you.

I agree to have my samples collected and used for research, and have some of my medical information (without personal identifiers) stored for research purposes:

Yes No Initials _____

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

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OTHER PERTINENT INFORMATION

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

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

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

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

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Geraldine O'Sullivan Coyne, MD, PhD, Building 31, Room 3A44, Telephone: 240-781-3371. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your tissue for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

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

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

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

Signature of Adult Patient/
Legal Representative

Date

Print Name

B. Parent's Permission for Minor Patient.

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

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

Signature of Parent(s)/ Guardian

Date

Print Name

C. Child's Verbal Assent (If Applicable)

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

Signature of Parent(s)/Guardian

Date

Print Name

**THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE
FROM MARCH 12, 2019 THROUGH APRIL 08, 2020.**

Signature of Investigator

Date

Signature of Witness

Date

Print Name

Print Name