The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	Testing Whether an Imaging Agent, Known as 18F-3'-deoxy-3'-[18F]-fluorothymidine (FLT) PET/CT, can predict who will have a good response to treatment in patients with pancreatic cancer
Version:	5
Official Study Title:	Initial evaluation of role of early interim 18F-FLT PET/CT for outcome prediction in pancreatic adenocarcinoma
Funding Agency/Sponsor:	UT Southwestern Medical Center
Study Doctors:	Dr. Daniella F. Pinho MD

You may call these study doctors or research coordinator during regular office hours at 214-645-1568. At other times, you may call them at 617-971-7982.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This study is being done to test if an imaging drug, not approved by the Food and Drug Administration (FDA), called FLT, is useful for evaluating your type of cancer and predicting how well your cancer responds to therapy. This drug is used with a PET/CT scan. PET is a nuclear medicine imaging technique that produces a '3-dimensional' image of processes occurring in the body such as breaking down of food, changing chemicals from one form into another and measure the amount of cells that are dividing, among others. A PET scan uses a small amount of a radioactive drug, or tracer, to show differences between healthy tissue and diseased tissue. The researchers want to see if the PET/CT scan, using the study drug, can improve assessing the treatment response early.

Why is this considered research?
This is a research study because fluorothymidine, also identified as FLT, is

investigational and has not been approved by the U.S. Food and Drug Administration (FDA) for the imaging of pancreatic cancer. The researchers are interested in learning if this procedure is effective to predict response to treatment in your condition/disorder.

The following definitions may help you understand this study:

- Standard medical care means that regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.

Why am I being asked to take part in this research study?

You are being asked to take part in this study because you are planning to begin chemotherapy or chemoradiation treatment for pancreatic adenocarcinoma. Your treating physician has determined that your treatment plan makes you eligible for the experimental imaging being studied. The experimental parts of this imaging study are the agent called FLT and the imaging test called FLT PET/CT and optional FDG PET/CT (if participant does not have a standard of care FDG PET/CT or if done more than 30 days prior to enrollment and if participant agrees to have the scan performed). The agent is commonly known as "FLT" (^{18}F- fluorothymidine), which is a marker of the amount of tumoral cells that are dividing and growing. It is a radioactive substance that may "light up" where cancer is in your body.

Do I have to take part in this research study?"

No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study, it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?

This study will enroll about 20 participants at UT Southwestern Medical Center and Parkland Health and Hospital Services.

What is involved in the study?

If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

Screening Procedures

To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- Physical exam and medical history – standard care
- Biopsy to confirm that you have a pancreatic adenocarcinoma – standard care. No new biopsy will be performed, we will look into your medical record for previous biopsy result.
- Standard medical care studies – a computed tomography ("CAT scan") and/or Magnetic Resonance Imaging of the abdomen showing that you have a pancreatic cancer. We will look into your medical record to confirm you have had one and you will not repeat either a CT or MRI for this study. Your physician may order a CT or MRI during follow-up per standard of care. We will not be repeating the CT or MRI during follow-up either.
- Pregnancy test (urine or blood pregnancy test) within 7 days before your FLT-PET/CT scan, if you can still have children

Pre-treatment clinical PET/CT scan with fluorodeoxyglucose (FDG), an agent used for PET imaging. If not done as part of standard of care or if you had one and it was completed more than 30 days before joining the study, you will have the option to have another FDG-PET/CT scan done, which will be done at no charge to you or your insurance company. This FDG PET/CT will be used solely for research.

Procedures and Evaluations during the Research

You will have the following procedures during the research study:

- Pre-treatment experimental FLT PET/CT imaging study
- Optional pre-treatment FDG PET/CT imaging study
- FLT PET/CT imaging study during treatment (after 2nd cycle of chemotherapy)
- Follow up telephone call the day after FLT-PET/CT to see how you are feeling

Description of the PET/CT Scan:

PET is a nuclear medicine imaging technique that produces a 3-dimensional image of processes occurring in the body such breaking down of food, changing chemicals from one form into another and measure the amount of cells that are dividing etc. A PET scan uses a small amount of a radioactive drug, or tracer, to show differences between healthy tissue and diseased tissue. Before the PET scan, a small amount of the experimental tracer, FLT, is injected into a patient. The PET scanner detects the radiation given off by the FLT and produces color-coded images of the body that show both normal and cancerous tissue.

Currently, many PET scanners also include CT. This allows images of both anatomy (CT) and function (PET) to be taken during the same examination. A CT scanner is a special kind of X-ray machine. Instead of sending a single X-ray through your body as with ordinary X-rays, CT sends several beams out simultaneously through the body from different angles. The computer processes the results, displaying them as a 2-dimensional picture shown on a monitor. The PET-CT scanner is a large machine with a hole in the middle. It looks like a donut with a table in the middle.

The final results from this research study may be shared with your treating physician when the study is completed. Your experimental imaging results may be released to the treating physician for your review, at your and the treating physician's request. As FLT imaging remains experimental, the early imaging results are not yet fully understood. The experimental imaging results should not and will not change your treatment course and will not be part of the medical record. If we identify anything that is a safety issue on basis of review, we will notify referring physician.

Preparation for a FLT PET/CT Scan:

Preparation for FLT PET/CT Scans:

There are no eating or drinking restrictions for FLT PET/CT scanning. You may also take your medications according to your normal schedule.

During the Exam:

On the day of your scan, a small intravenous (I.V) catheter will be inserted into a vein of your hand or arm. You will receive a small injection of the radioactive drug FLT. The FLT will need to circulate around in your body for 50-70 minutes before your scan. During this time you will be asked to rest comfortably. FLT travels to places in the body where there is cellular proliferation. It shows up in cancer because cancer cells tend to proliferate more than normal tissues.

You will be asked to lie on the imaging table with your arms resting comfortably above your head or secured to your sides. You will move slowly through the scanner so that your body can be scanned from the head through the thighs. You will be asked to remain still for the scan which will take between 20-45 minutes to complete. The total amount of time you will need for the FLT PET/CT scan is approximately 2-3 hours.

A repeat FLT PET/CT scan will be performed after completion of the 2nd cycle of chemotherapy. Researchers would use this scan to evaluate if the changes compared to the first study (before treatment) can predict which patients will have a longer survival and who will be eligible for surgery after completion of 6 cycles of treatment. This would involve an additional visit after completion of the 2nd cycle of chemotherapy to have the FLT-PET/CT imaging scan. This would involve requiring an IV to give you the FLT imaging agent. The scan would only be used for research and not to guide your medical care.

Treatment: After you have had your second FLT PET/CT scan, you will complete chemotherapy regimen. The therapy that you will receive is not a part of this study. It will be the standard of care treatment for your type of cancer. You will continue to see your treating oncologist and response of your cancer to chemotherapy will be evaluated according to standard of care.

You will see your treating doctor at regular intervals according to her/his recommendations. Information gathered by your treating doctor as part of your normal

follow-up visits will be given to your study doctor(s) for approximately two years so they can find out more about your health. Your follow-up care will be decided between you and your treating doctor

Optional Section:

Optional FDG-PET/CT

FDG PET/CT is FDA approved and participants who do not have one done as Standard of care within 30 days of ^{18}F FLT may choose to participate in this section, otherwise FDG PET/CT will not be required.

Preparation for FDG-PET/CT Scan:
You will be asked not to eat anything for 4-6 hours before your appointment and to drink only plain water. Check with your study doctor to make sure it is alright to take medications, especially if you are a diabetic.

During the Exam:
On the day of your scan, a small intravenous (I.V) catheter will be inserted into a vein of your hand or arm. This I.V catheter will be used to draw a small blood sample (less than 1 teaspoon) to check the amount of sugar (glucose) present in your blood stream. If your blood sugar is okay, you will receive a small injection of the radioactive drug FDG (a radioactive form of sugar). If your blood sugar is not within the proper range, we may not be able to perform the FDG-PET/CT exam on this day. You will be asked to follow a diet, which is low in sugars and carbohydrates and return to the PET facility on another day. The FDG will need to circulate around in your body for 50-70 minutes before your scan. During this time you will be asked to rest comfortably. FDG travels to places in the body where glucose is used for energy. It shows up in cancer because cancer cells use more glucose than normal tissues. Before the start of your scan you will be asked to use the restroom. About 10-30 minutes after you have been given the FDG, you may be asked to drink approximately 20 ounces of an FDA-approved oral contrast material used in CT scanning that makes it easier to see your intestines on the pictures. About 30 minutes after you drink the oral contrast you will be asked to lie on your back on the PET imaging table for pictures.

You will be asked to lie on the imaging table with your arms resting comfortably above your head or secured to your sides. You will move slowly through the scanner so that your body can be scanned from the head through the thighs. You will be asked to remain still for the scan which will take between 20-45 minutes to complete. The total amount of time you will need for the FDG PET/CT scan is approximately 2-3 hours.

I would like to participate in the optional FDG PET/CT study:

Yes	No

How long can I expect to be in this study?
You will be done with the study procedures after you have the two FLT-PET/CTs (one before starting treatment and one after the 2nd cycle of chemotherapy), and someone will call you the day after your imaging tests to see how you are doing. Then information will be collected about your response to treatment for the study for about two years.

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. In some cases, side effects can be serious, long lasting, or may never go away. Some side effects may be lethal. You should talk to your study doctor about any side effects that you have while taking part in the study.

Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Possible side effects related to the PET/CT scan:

- Anxiety / stress / Claustrophobia (extreme fear of confined places).

Possible side effects related to the I.V needle placement likely:

- Discomfort from the I.V and injection of FLT into your vein
- Discomfort from lying still for imaging (typically about 30-60 minutes)

- Less Likely / Less Common:
    - Swelling
    - Bleeding
    - Infection
    - Bruising

<u>Risks and side effects related to the drug used for PET (called FLT):</u>
Rare but serious:

- There is a rare possibility of an allergic-type or other adverse reaction to the radioactive labeled tracer FLT. Such a reaction could be serious or life-threatening.

No other side effects have been reported after injection on the amount of FLT that will be used in this study.

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

Risks of Radiation – Diagnostic Test

This research study includes exposure to radiation from diagnostic tests in addition to that which you would receive from standard care. The risk of harm to your body from this radiation can be compared to risks from everyday activities. For example, the risk of developing fatal cancer during your lifetime from this radiation is comparative to the risk of suffering a fatal car crash while driving 2,300 miles (5,330 miles if FDG is not performed as standard of care) in an automobile. The average household in the United States drives 23,000 miles per year (2001 data).

Reproductive Risks:

If you are a woman of childbearing potential, please read the information in the box and sign below indicating your understanding of this information on reproductive risk.

Because PET/CT scans can be harmful to an unborn baby, you should not become pregnant while on this study. There is not enough medical information to know what the risks might be to an unborn child in a woman who takes part in this study. It is important that you understand that you need to use birth control while on this study. Ask your study doctor about what kind of birth control methods to use and how long to use them. If you are a woman who can become pregnant, you must agree to a pregnancy test (blood or urine test) within 7 days before the FLT PET/CT scan (or FDG if not provided as standard of care or done more than 30 days prior to enrollment and agree to the optional sectional).

Risks to Sperm, Embryo, Fetus or Breast-fed Infant

Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control. Medically-acceptable forms of birth control include:

(1) Surgical sterilization (vasectomy), or
(2) A condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a blood pregnancy test or urine pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick or urine), and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control

(contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

(1) Surgical sterilization (such as hysterectomy or “tubes tied”),

(2) Approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),

(3) Barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or

(4) An intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately. Radiation exposure to a woman’s reproductive organs may harm an embryo or fetus. Also, if radioactive materials are used for certain types of scans, harm may come to an embryo, fetus, or an infant who is breast feeding.

Pregnancy tests performed during the early stages of pregnancy do not always reveal pregnancy. Therefore, radiation exposure that includes the reproductive organs will be limited to the first ten days after a woman who can become pregnant has begun her most recent menstrual period. This is standard policy in clinics and hospitals within UT Southwestern. This policy applies unless there is an important medical reason requiring radiation outside this time frame.

I will use an accepted and effective method of contraception or abstain from sexual intercourse for the duration of the study.

Yes	**No**

Risks of Blood Drawing

Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely. You will have the same amount of blood collected whether you receive standard medical care for your health problem or take part in this research. You will have less than 6 teaspoons of blood collected because you are in this research study.

Other Risks

There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

Loss of Confidentiality

Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

How will risks be minimized or prevented?
Potential risks and discomforts will be minimized to the greatest extent possible by using procedures such as appropriate training of personnel, monitoring, withdrawal of subject participation upon evidence of difficulty or adverse event; referral for treatment, counseling or other necessary follow-up.

What will my responsibilities be during the study?
While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illnesses while you are on study, even if you do not think that the event is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research, because we do not know if the study imaging is effective for predicting response to therapy. The results from the FLT-PET/CT will not be shared with you or your treating doctors, unless both your treating physician and you specifically request. This research study may help researchers learn things that may help other people in the future.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- You may choose to not undergo the imaging study, and would then have the usual routine care
- You may choose to take part in a different research study, if one is available

Please talk to the researchers or your personal doctor about these options.
This is not a treatment study. You do not have to be part of it to get treatment for your condition.

Will I be paid if I take part in this research study?
No. You will not be paid to take part in this research study. There are no funds available to pay for parking expenses, transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas or Parkland Health and Hospital Services.

You retain your legal rights during your participation in this research

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff/Parkland Health and Hospital Services or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.
- National Cancer Institute (NCI).

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by the 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.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Are there procedures I should follow after stopping participation in this research?
Yes. If you, the researchers, or the sponsor stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for tests that may be needed for your safety.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

Whom do I call if I have questions or problems?
For questions about the study, contact Dr. Daniella Pinho at 214-645-1568, during regular business hours and at 214-786-4703 after hours and on weekends and holidays.
For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES: YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.

_____
Name of Participant (Printed)

_____ _____ _____ AM / PM
Signature of Participant Date Time

_____
Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM
Signature of Person Obtaining Consent Date Time

Interpreter Statement:

I have interpreted this consent form into a language understandable to the participant and the participant has agreed to participate as indicated by their signature on the associated short form.

_____

Name of Interpreter (Printed)

_____ _____ _____ AM / PM

Signature of Interpreter Date Time