FOX CHASE CANCER CENTER
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FOX CHASE CANCER CENTER
AT TEMPLE UNIVERSITY HOSPITAL
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INFORMED CONSENT DOCUMENT

A Phase Ib/II Study of the Safety and Activity of Digoxin with Decitabine in Adult AML and MDS

Supported by: Fox Chase Cancer Center

Principal Investigator: Dr. Philip Pancari

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You should discuss your decision with your friends and family. You will also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this research study because you either have newly diagnosed or relapsed/refractory AML (Acute Myeloid Leukemia) or MDS (Myelodysplastic Syndrome. MDS/AML is a form of cancer of blood and bone marrow in which bone marrow does not produce enough healthy blood cells.

The sponsor of this study is Fox Chase Cancer Center.

Why is this research study being done?

The purpose of this research study is to:

- Test different doses of digoxin with standard dose of decitabine to find which dose is safer in patients with newly diagnosed or relapsed/refractory AML/MDS. Digoxin is not normally used in the treatment of AML/MDS. Digoxin is approved by Food and Drug Administration (FDA) to treat heart failure. Adding digoxin to your treatment is considered experimental
- Test if the combination of digoxin and decitabine is safe and effective in treating patients with newly diagnosed or relapsed/refractory AML/MDS.

How many people will take part in this research study?

Up to 100 people will take part in this research study.

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

Screening before you begin the research study

You will need to have the following exams, tests or procedures to find out if you can be in the research study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the research study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- We will ask you about your medical history
- We will do a physical exam and vital signs
- We will ask about your ability to do your daily activities
- Routine blood tests (1 tablespoon)
- Blood pregnancy test (2 teaspoon), if you are a female and able to become pregnant.
- We will evaluate your cancer by doing a bone marrow biopsy
- We will check your heart by performing an EKG.
    - EKG is a test to measure the electrical activity of your heart

During the research study

If the exams, tests and procedures show that you can be in the research study, and you choose to take part, then you will take study treatment and you will need some tests and procedures.

- We will ask you about the medicine you are taking
- We will do a physical exam and vital signs
- We will ask about your ability to do your daily activities
- Routine Blood tests (1 tablespoon).
- We will check your heart by performing an EKG.
- We will ask you about any side effects you may be experiencing
- We will evaluate your cancer by doing a bone marrow biopsy at the end of cycle 3 and cycle 6
- Blood for research – 9 times during the study (2 tablespoons/time-point). Blood will be collected on days 1, 6, 13, 21 of cycle 1 and 2 and once on day1 of cycle 3.

This study has two phases: Phase Ib is to determine the combination dose of decitabine and digoxin that is safe and tolerable, while Phase II is to determine the efficacy of the combination treatment. Phase Ib portion of the study will only have 1 cycle while Phase II portion of the study will have a up to 6 cycles.

Randomization

If you are enrolled in Phase II portion of this study you will be randomized into one of the two groups. Patients in group A will receive decitabine alone while patients in group B will receive decitabine with digoxin. Randomization means that you will be placed in a group by a computer program by chance and neither you nor your study doctor can decide which group you will be place in. You will have equal chance of being in one of the research groups. Patients in group A will receive decitabine alone only for cycle 1. Starting from cycle 2 patients in group A will also receive decitabine with digoxin.

Treatment

You will receive a one-time only loading dose of digoxin, to be taken orally on day 1 and then you will be asked to take digoxin orally every day from day 2 through day10 of a 28 days cycle, for a total of 6 cycles. In addition you will be administered decitabine through your vein over 1 hour every day from day 6 through day10 of a 28 days cycle, for a total of 6 cycles.

Possible use of a port

If the doctors or nurses cannot draw blood or give you medicine through your veins, you may be asked to have minor surgery to place an "indwelling catheter port" into a large vein in your chest. Medical staff will use the "port" to give you medicines and to draw blood. You will be asked to sign a separate consent form for this procedure, and the "port" will not be used unless you agree. If a port is necessary and you do not agree to its use, you may be unable to continue as part of the research study.

After you stop taking the study drug

We will perform the following when you discontinue the study treatment

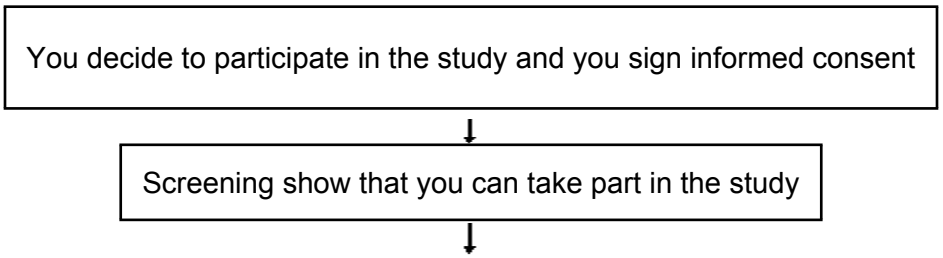
- We will ask you about the medicine you are taking
- We will do a physical exam and vital signs
- We will ask about your ability to do your daily activities
- Routine Blood tests (1 tablespoon).
- We will check your heart by performing an EKG.
- We will ask you about any side effects you may be experiencing

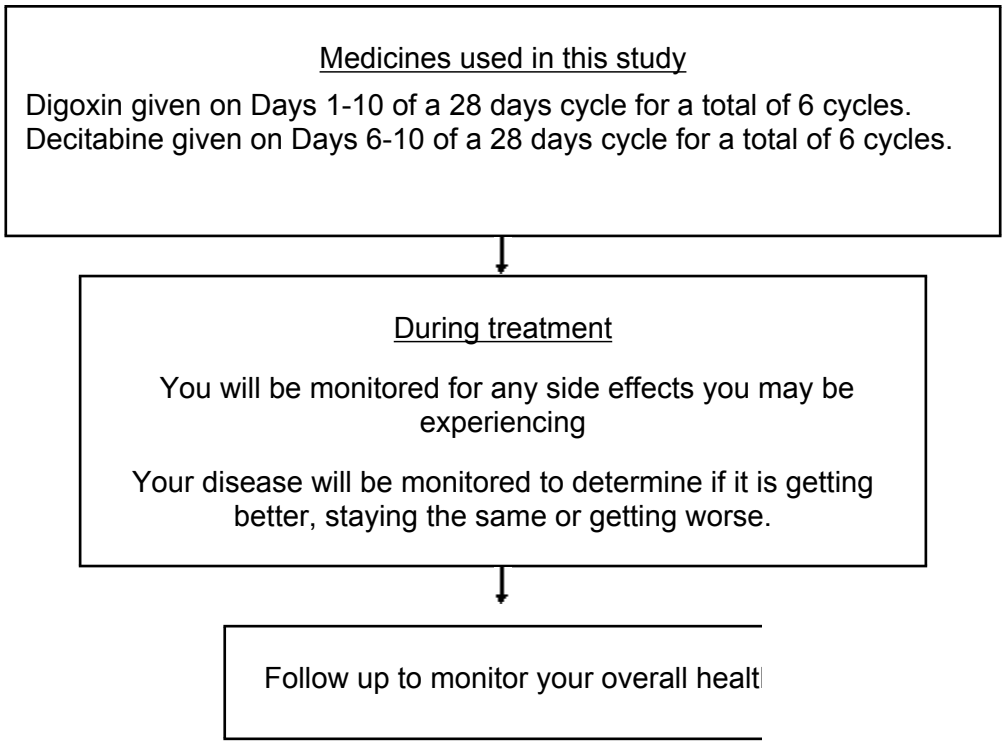
Follow-Up

After you are finished taking the study drug, we will perform a safety follow-up, 30 days after discontinuation and ask you about any side-effects that you may be experiencing. We will monitor your cancer by assessing your blood every month for 6 months after discontinuation. After that we would follow up with you every month for 6 months by phone call to monitor your overall health.

Study Plan

Another way to find out what will happen to you during the research study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.





How long will you be in the research study?

You may be in the study for approximately 12 months, or until your disease gets worse or you experience intolerable side effects.

Can you stop being in the research study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drugs can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Can you be removed from this research study?

The study doctor may stop you from taking part in this research study at any time if he/she believes it is in your best interest; if you have side effects that you cannot tolerate; if you do not follow the research study rules; or if the research study is stopped.

What side effects or risks can you expect from being in the research study?

You may have side effects while on the research study. Everyone taking part in the research study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may

give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drugs. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the research study.

Risks and side effects related to **decitabine** include those which are:

Likely (≥ 20%)

- Leukopenia/Neutropenia: (low white blood cell count) A low white blood cell count makes it hard for you to fight infections
- Thrombocytopenia (low platelet count) Platelets are important in stopping bleeding. A low platelet count can increase and prolong bleeding
- Anemia (low hemoglobin, low hematocrit or low red blood cell count) Red blood cells carry oxygen and nutrients throughout the body. Symptoms that may be experienced as a result of low red blood cell counts may include feeling tired and weak, shortness of breath, increased heart rate, dizziness or lightheadedness, headache, chest pain and pale skin
- Superficial bleeding under the skin which results in pin point flat round red spots
- Headache
- Constipation (difficulty having a bowel movement)
- Nausea (feeling sick to your stomach)
- Vomiting (throwing up)
- Diarrhea
- Cough
- Fever
- Chills
- Joint/muscle pain
- Fatigue (feeling of being overly tired and lacking energy)
- Insomnia (difficulty sleeping or falling asleep)
- Hyperglycemia (high blood sugar) Symptoms of high blood sugar may include increased hunger, increased thirst, dry mouth and increased urination
- Hypomagnesemia (low magnesium level in the blood) – symptoms may include muscle cramps, weakness, tremors and abnormal heart beats
- Hypokalemia (low levels of potassium) – symptoms may include muscle weakness, cramping, leg discomfort, an irregular heart beat and confusion
- Hyperkalemia (elevated levels of potassium) – symptoms may include nausea, diarrhea, fatigue, muscle weakness or a tingling sensation, chest pain and heart palpitations
- Hypocalcemia (low calcium levels in the blood) – symptoms of a low calcium level may include numbness and tingling in the hands and feet, muscle cramps, twitches and spasms, fatigue, confusion, disorientation and seizures.
- Hypoalbuminemia (low levels of albumin in the blood) – albumin is a protein that is found in the blood. Low levels of albumin may produce no symptoms, unless your blood albumin levels are very low. Symptoms associated with low albumin may include poor appetite, swelling that is all over the body or in a certain part of the body such as the legs or abdomen, muscle weakness, fatigue or cramps.
- Peripheral edema – swelling of the hands, feet, ankles, or lower legs

- Hyponatremia (low sodium levels in the blood) – symptoms may include nausea and vomiting, loss of appetite, headache, confusion, fatigue, restlessness and irritability, muscle weakness, spasms or cramps, decreased consciousness, seizures or coma.

Less Likely (between 5% and 19%)

- Anxiety
- Confusion
- Dizziness
- Blurred vision
- Rash
- Itching
- Mucositis/stomatitis – sore in the lining of your mouth and/or throat that can be painful and make it hard to swallow
- Indigestion
- Stomach pain
- Loss of appetite
- Shortness of breath
- Hypotension (low blood pressure) – you may experience dizziness or feel like you are going to pass out
- Heart murmur
- Chest pain
- Fast heart rate
- Hair loss
- Elevated liver enzymes – liver enzymes are proteins made by the liver that are measured in the blood, with a blood draw. Liver enzymes indicate how well your liver is functioning. Elevated liver enzymes may cause no symptoms, however higher liver enzyme levels may cause you to feel overly tired or weak, you may bruise or bleed more easily, and you may experience abdominal pain or have a yellowing of the skin or eyes.

Rare But Serious (< 5%)

- Kidney damage
- Heart failure – a lowered ability of the heart to pump blood
- Infections
- Severe bleeding in the brain

Risks and side effects related to **digoxin** include those which are:

- Changes in heart rhythm, including irregular heartbeat
- Fast or slow heartbeat.
- Facial swelling
- Dizziness
- Changes in mood and mental alertness, including confusion, depression and lost interest in usual activities
- Anxiety
- Headache
- Fever
- Hallucinations (seeing or hearing things that are not there)
- Rash and itching

- Nausea, vomiting and diarrhea
- Belly pain
- Not hungry
- Weakness
- Visual problems, including blurry vision and yellow halos
- Growth or enlargement of breast tissue in men (gynecomastia) (< 1%)
- Low platelet count (< 1%)

Signs of Digoxin Toxicity
Signs of digoxin toxicity include inability or unwillingness to eat (anorexia), nausea, vomiting, and/or new visual changes such as double vision or blurriness. Palpitations (the sensation of your heart pounding within your chest) may indicate an abnormal heart rhythm brought on by the digoxin.

Patients at greatest risk for digoxin toxicity include those with very low body weight, those who are very elderly, those with pre-existing kidney damage, and those with a history of difficulty maintaining normal electrolyte levels (potassium, calcium or magnesium).

If you experience persistent or repeated vomiting, sudden changes in your vision, palpitations or chest pain, you should call for immediate medical help.

Blood Draw Risks
- Fainting
- Bleeding at the site of blood draw
- Bruising at the place on your arm where the blood was drawn or needle inserted
- Pain at the site of blood draw
- Swelling at the site of blood draw
- Infection (rare)

Biopsy Risks
- Bleeding
- Pain
- Infection, which can be life-threatening or fatal in rare cases

Reproductive Risks

- Study treatments may make you sterile (unable to have children).
- The drugs in this study may affect a baby, before or after the baby is born.
- You should not become pregnant or father a baby while on this research study because the drugs you take could possibly hurt an unborn baby.
- If you are pregnant now or if you are breast-feeding now, you may not take part in this research study.
- If you become pregnant while you are on the research study, you may not continue to take part in the research study.

<u>For women who can become pregnant</u>:
- You should not become pregnant while you are in this study.
- You should not breast-feed your baby while taking drugs for this research study.

- If you are having sex that could lead to pregnancy, you should use birth control during the study and for at least 3 months after the end of study treatment.

For men:

- You should not make a woman pregnant while you are in this study.
- If you are having sex that could lead to pregnancy, you should use birth control during the study and for at least 2 months after the end of study treatment.

For women and men:

- Check with the study doctor about birth control methods. Some methods might not be approved for use in this study.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. It is possible that your condition will get better, but it is also possible that there will be no effect on your condition or that your condition will get worse. While doctors hope that the combination of digoxin and decitabine will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about the combination of digoxin and decitabine as a treatment for cancer. This information could help future cancer patients.

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

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part 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. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Fox Chase Cancer Center and affiliated Joint Centers, The Institutional Review Boards of The Fox Chase Cancer Center and Temple University, Temple University, Temple University Health system, Inc., and its affiliates or subsidiaries and other authorized representatives of these organizations.

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

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 will be given a separate form to review regarding the steps we will take to guard your privacy as part of your participation in the research study. By signing that additional authorization, you will be providing your consent to use and disclose information described in that form connected with your participation in this research study.

What are the costs?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

Fox Chase Cancer Center will provide digoxin at no charge while you take part in this study.

You or your health insurance company will need to pay for decitabine, check with your health plan or insurance company to find out if they will pay for decitabine.

If your insurance will not pay for medicines you may need to help with side effects, you may have to pay for them.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

Will you be compensated?

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

What if you are injured while taking part in this research study?

If you are injured as a result of your participation in this research study, seek immediate medical care. Temple University Health System or its subsidiaries will treat the injury, though there is no commitment to provide monetary compensation or free medical care. Other financial compensation (such as lost wages or pain and suffering) for such injuries is not available.

What are your rights if you take part in this research study?

Taking part in this research study is your choice. You may choose either to take part or not to take part in the research study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not

lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

New findings

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

Who can answer your questions about the research study?

Important Contact Numbers	
If you have questions about:	Please Call:
This study, including if you get sick or hurt	Dr. Philip Pancari at 215-728-4300
If you have a concern or complaint	Risk Management Department at 215-728-2591
Your rights as a research participant on this study	FCCC Institutional Review Board at 215-214-3754
Your bills or health insurance coverage	Clinical Trial Financial Counselor at 215-214-3768

Where can you get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI website at http://cancer.gov

- For NCI's clinical trials information, go to: http://cancer.govclinicaltrials/
- For NCI's general information about cancer, go to: http://cancer.gov/cancerinfo/

By signing below, you tell us that you have gotten all of the information you need; that you have received clear answers to your questions, and that you agree to take part in the research study. You will receive a copy of this form. You may also request a copy of the research plan.

Signature of Participant	Print Name of Participant	Date

By signing this form the Physician obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Physician	Print Name of Physician	Date

Obtaining Consent **Obtaining Consent**

By signing this form the person obtaining consent indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Person Obtaining Consent	**Print Name of Person Obtaining Consent**	**Date**

Signature of Legally Authorized Representative (LAR)	**Date**

Print Name of LAR	**Relationship of LAR to Participant**

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under the Commonwealth of Pennsylvania)

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Authorization (Permission) to Use or Disclose (Release) Protected Health Information (PHI) for Research

IRB# and Protocol ID: **16-1061**
Study Title: **HM-091: A Phase Ib/II study of the safety and activity of Digoxin with Decitabine in adult AKL and MDS**

Principal Investigator: Philip Pancari, MD
Sponsor: Philip Pancari, MD at Fox Chase Cancer Center

1. What is the purpose of this form?

This form is required by the Health Insurance Portability and Accountability Act of 1996. Specifically the privacy regulation (HIPAA) permits the research investigators listed above to use and disclose health information about you for the research study identified above which has been approved by the Fox Chase Cancer Center Institutional Review Board.
The sponsor is an organization/person that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your protected health information for research. The elements of protected health information as defined by HIPAA are:

Data Elements for Protected Health Information (PHI)

- Names
- All geographic subdivisions smaller than a state (except for the first 3 digits of the zip code in some cases)
- All elements of dates (except year) for dates directly related to an individual (e.g., birth date, admission date, discharge date, date of death) and all ages over age 89 and dates indicative of that age
- Telephone numbers
- Fax numbers
- E-mail addresses
- Social security numbers
- Medical record numbers
- Health plan beneficiary numbers
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Device identifiers and serial numbers
- Web Universal Resource Locators (URL)
- Internet Protocol (IP) addresses
- Biometric identifiers, including finger and voice prints
- Full face photos and any comparable images

- Any other unique identifying number, characteristic, or code

2. What protected health information do the researchers want to use?
The researchers want to copy and use the portions of your medical record that they will need for their research. If you enter a research study, medical information that will be used and/or released may include the following:

- The history and diagnosis of your disease
- Specific information about the treatments you received, including previous treatment(s) you may have had
- Information about other medical conditions that may affect your treatment
- Medical data, including laboratory test results, tumor measurements, CT scans, MRIs, x-rays, and pathology results
- Long-term information about your general health status and the status of your disease
- Data that may be related to tissue, urine and/or blood samples that may be collected from you

You may request a blank copy of the data forms from the study doctor or his/her research staff to learn what information will be shared.

3. Why do the researchers want my protected health information?
Fox Chase Cancer Center will collect your protected health information and share it with the sponsor, as applicable, if you enter a research study. The centers will use your information in their cancer research study.

4. Who will be able to use my protected health information?
Fox Chase Cancer Center, Temple University, Temple University Health System affiliates, and Temple University Clinical Faculty Practice Plan will use your health information for research. As part of this research, they may give your information to the following groups taking part in the research. Fox Chase Cancer Center and Temple University may also permit these groups to come in to review your original records that are kept by Fox Chase Cancer Center so that they can monitor their research study.

- The Fox Chase Cancer Center IRB
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law
- Other people or organizations assisting with research efforts of the sponsor
- Central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed above

5. How will information about me be kept private?
The sponsor will keep all patient information private to the extent possible, even though the sponsor is not required to follow the federal privacy laws. Only researchers working with the sponsor will have access to your information. The sponsor will not release personal health information about you to others except as authorized or required by law. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected. However, the laws of the Commonwealth of Pennsylvania or your state of residence may provide further privacy protection.

6. What happens if I do not sign this permission form?
If you do not sign this permission form, you will not be able to take part in the research study for which you are being considered.

7. If I sign this form, will I automatically be entered into the research study?
No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a specific research consent form.
Treatment by your physician will not be affected by whether you provide authorization for the requested use or disclosure except if your treatment is related to research.

8. What happens if I want to withdraw my permission?
You can change your mind at any time and withdraw your permission to allow your protected health information to be used in the research. If this happens, you must withdraw your permission in writing. Beginning on the date you withdraw your permission, no new protected health information will be used for research. However, researchers may continue to use the protected health information that was provided before you withdrew your permission. If you sign this form and enter the research study, but later change your mind and withdraw your permission, you will be removed from the research study at that time.

To withdraw your permission, please contact the person below. She will make sure your written request to withdraw your permission is processed correctly.

Contact Name:	Philip Pancari, MD
Contact Address:	333 Cottman Avenue Philadelphia, PA 19111
Contact Phone and FAX:	215-728-4300 and 215-728-3639

9. How long will this permission last?
If you agree by signing this form that researchers can use your protected health information, this permission has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

10. What are my rights regarding access to my personal health information?
You have the right to refuse to sign this permission form. You have the right to review and/or copy records of your protected health information kept by Fox Chase Cancer Center and Temple University affiliates. However, while the research study is in progress, you may not be able to access your protected health information in order to preserve the integrity of the research. You will be able to access this information when the study is completed. You do not have the right to review and/or copy records kept by the sponsor or other researchers associated with the research study.

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Signatures
I agree that my protected health information may be used for the research purposes described in this form.

Signature of Participant	**Print Name of Participant**	**Date**

By signing this form the physician indicates that the research participant has been fully informed of all aspects of the research study.

Signature of Physician	**Print Name of Physician**	**Date**

Signature of Person Obtaining Consent	**Print Name of Person Obtaining Consent**	**Date**

Signature of Legally Authorized Representative (LAR)	**Date**

Print Name of LAR	**Relationship of LAR to Participant**

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under the Commonwealth of Pennsylvania)

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