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Consent for Cancer Research

Project Title: CASE6220: A Phase II, Randomized, Double-Blind Trial Comparing Escitalopram to Placebo in Patients with Localized Pancreatic Cancer

Sponsor: Case Comprehensive Cancer Center (Case CCC)

University Hospitals Principal Investigator: Jordan Winter, MD

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at University Hospitals (UH).

Key Information: The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?
We invite you to take part in a research study because you have been diagnosed with pancreatic cancer and could be at risk for or have developed depression. Your doctor has planned for you to have at least 12 weeks of chemotherapy.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?
The purpose of this study is to find out if a drug called escitalopram is effective in preventing or reducing depression and improving quality of life in people who have been diagnosed with cancer of the pancreas.

Escitalopram is a drug that works by increasing the amount of a chemical called serotonin in the brain. Having more serotonin helps decrease the symptoms of depression and anxiety. Escitalopram is approved by the U.S. Food and Drug Administration (FDA) for the treatment of diagnosed major depressive disorder in adults and adolescents. Escitalopam is experimental because it is not approved by the Food and Drug Administration (FDA) to prevent or reduce depression in adults with cancer of the pancreas.

How long will the research last and what will I need to do?
You will receive Escitalopram for about 12 weeks and you will have a follow-up visit at Week 25. You will be asked to take escitalopram or placebo (an inactive pill) by mouth every day for about 12 weeks. You and your doctor will not know if you are taking escitalopram or placebo. You will give a blood sample. You will be asked to complete a pill diary while you are taking the

medication. You will be asked to complete questionnaires while you are on treatment. The questionnaires ask about how you are feeling, if you are having side effects and if you feel depressed.

More detailed information about the study procedures can be found under "What extra tests and procedures will I have if I take part in this study?"

Is there any way being in this study could be bad for me?
If you are on this study you might have more side effects in addition to side effects from your treatment for cancer of the pancreas. You may feel uncomfortable answering some of the questions about how you feel physically and if you feel depressed. The two most serious side effects of the drug are restlessness and thoughts or plans of suicide.

More detailed information about the risks of this study can be found under "What possible risks can I expect from taking part in this study?"

What possible benefits can I expect from taking part in this study?
We cannot know if you will have any benefit as a result of your participation in the study. The potential benefit of participation include prevention of depression, improved quality of life, and improved cancer survival.

Your participation in this study will help to obtain information about treating and preventing depression in other patients with cancer of the pancreas in the future.

What are my other choices if I do not take part in this study?
You have the option not to take part in this study. You will still be treated for your cancer of the pancreas if you decide not to be in this study.

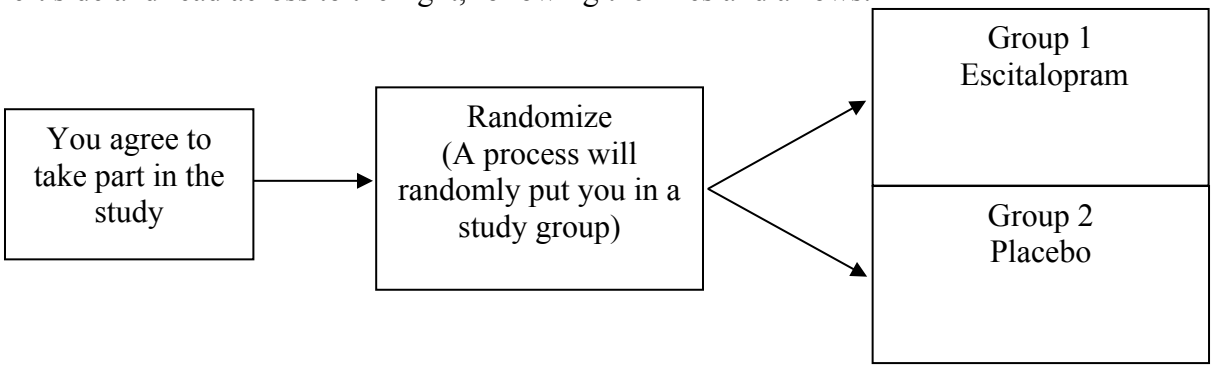
Detailed Information: The following is more detailed information about this study in addition to the information listed above.

What are the study groups?
This study has two study groups. Group 1 will receive the study drug escitalopram and Group 2 will receive a placebo, a pill that looks like the study drug but contains no medication. There will be 23 patients in each study group.

A process will be used to assign you, by chance, to one of the study groups. Neither you nor your doctor can choose which group you are in. This is done by chance because no one knows if one

study group is better or worse than the other. You and your study doctor will not know which group you are assigned to.

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



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

You will be asked to do the following if you agree to take part in this study.

Blood samples: Before you start your treatment on this study, you will have blood drawn (about 5 teaspoons). If you have surgery to remove your tumor after your chemotherapy, you will have these blood samples drawn again 1 to 3 months after you have your surgery. These samples will provide information about how the escitalopram or placebo is being broken down by your body. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study.

Tumor samples: This is a laboratory test performed on a piece of tissue from your tumor that was taken for your cancer. If you have surgery to remove your tumor, we will request this sample in order to perform tests that provide information about your cancer. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study.

Questionnaires: About every two weeks you will be asked to complete questionnaires. The questionnaires ask about side effects, how your cancer and treatment affects your daily activities and social life, and whether or not you are feeling depressed. It may take up to a half an hour to complete these questionnaires.

The questionnaires will be completed at the time of a scheduled chemotherapy visit or over the telephone with a member of the study staff. These questionnaires are:

-FACT-Hep: This is a quality of life questionnaire that asks about how your cancer and treatment are making you feel physically and emotionally and how your cancer and treatment are affecting your daily life.

-QIDS: These are brief surveys designed to find out if you are having symptoms of Depression

-PHQ-9: This is a short survey that asks questions about your health and is designed to find out if you are having symptoms of depression.

-FIBSER: This questionnaire is a short questionnaire asking about side effects of depression medication.

You will be screened to determine if you meet the qualifications for this study. It is important that you tell your study doctor or the research staff if you have any history of psychiatric illness, mania or bi-polar disorder.

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

- Medical history: a discussion or a review of your medical record to receive information about your health, any treatments you have received for your cancer, and information related to your diagnosis.
- Physical examination to include an ECG (electrocardiogram) to measure your heart rhythm.
- Performance status: an evaluation of your ability of care for yourself and function day to day
- Pregnancy test

During the study the following will be additional research procedures:
<u>Week 1, Day 1 (clinic visit):</u>

- Performance status
- Blood samples for research studies (about 5 teaspoons)
- FACT-Hep
- QIDS-SR baseline survey
- PHQ-9
- FIBSER
- You will receive a 2-week supply of escitalopram/placebo pills
- You will receive a pill diary to record when you take your pills

Daily x12 weeks* :

- You will take 1 pill (10mg/day) on Days 1-14 (Weeks 1 and 2)
- You will take 2 pills (20mg/day) on Days 15-70 (Weeks 3 through 10)
- You will take 1 pill (10mg/day) on Days 71-84 (Weeks 11 and 12)

* (you will need to come to the clinic on Day 15 and Day 71 to return your pill diary to your study nurse and to receive your next supply of escitalopram).

Every 2 weeks (phone call or clinic visit):

- QIDS-SR
- PHQ-9
- FIBSER
- Review of side effects
- Review of pill diary

Once per month (phone call or clinic visit):

- FACT-Hep

Week 13 (clinic visit):

- Pill diary will be collected
- Medical History
- Physical exam
- Performance Status
- QIDS-SR
- PHQ-9
- FIBSER
- FACT-Hep
- Review of side effects

Week 25 (phone call or clinic visit)

- QIDS-SR
- FIBSER
- PHQ-9
- FACT-Hep
- Review of side effects

Every 12 weeks for three years

- We will follow you by review of your medical records for three years to assess the status of your disease and whether or not you have additional treatment for your cancer.
- If you have surgery to remove your tumor we will request a blood sample for research studies one to three months after your surgery.

If you need to stop taking escitalopram/placebo before you complete all the study visits you will be asked to continue with your study visits/phone calls and complete the questionnaires. If you have surgery, your tumor and blood samples will still be used for research purposes.

What possible risks can I expect from taking part in this study?
If you choose to take part in this study, there is a risk that:

- You may be asked sensitive or private questions which you normally do not discuss

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important points about side effects:

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

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

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects 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 escitalopram:

VERY COMMON, SOME MAY BE SERIOUS In 100 people receiving escitalopram, more than 30 and up to 100 may have:
• Restlessness or agitation

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving escitalopram, from 5 to 12 may have:
• Dry Mouth • Nausea

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving escitalopram, from 5 to 12 may have:
• Dizziness • Decreased appetite • Drowsiness

RARE, AND SERIOUS **In 100 people receiving escitalopram, 3 or fewer may have:**
• Fatigue • Bleeding • Trouble sleeping • Headache • Diarrhea • Heartburn • Constipation • Excessive sweating • Irregular heartbeat • Pressure in the chest • Bloating • Stomach discomfort • Upper respiratory infection • Head distension • Excessive yawning • Palpitation • Physical discomfort • Suicide attempt

Serotonin Syndrome: This is a serious condition that is most likely to occur in patents who are taking other drugs that increase levels of serotonin at the same time they are taking escitalopram. Symptoms of Serotonin Syndrome include agitation, confusion, restlessness, headache, vomiting, diarrhea, tremors, loss of muscle control, high fever, sweating and seizures.

The two most serious side effects of the drug are restlessness and thoughts or plans of suicide.

Other minor side effects such as GI discomfort usually go away on their own, and ALL side effects will go away if the medication is stopped.

If you experience any side effects, please call the lead investigator who may refer you to the study psychiatrist and possibly remove you from the trial.

If you have thoughts of hurting yourself, you will immediately be referred for help.

If you should have thoughts of hurting yourself, we urge you to call your physician _____ at _____. If you feel you need to call your physician after business hours you should call [redacted] and you will be put in touch with your doctor or the oncologist (cancer doctor) on call.

You can also communicate this feeling to the study staff at a study visit or via telephone when you complete the study forms which are administered every 2 weeks.

Be sure to tell you study doctor, nurse, or study staff if you are taking any drugs that may increase your risk of bleeding. These include blood thinners (such as warfarin, Coumadin, Xarelto or other anti-coagulants). You should also discuss the use of aspirin and NSAIDS such as ibuprofen (Motrin, Advil) and naproxen (Aleve) with your study doctor or nurse as these medications may increase your risk of bleeding.

Potential Risk or Discomfort from Research Procedures

Blood Draws
The insertion of the needle to draw blood is painful; however, the discomfort is usually brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

Questionnaires (QIDS, FACT-Hep., FIBSER Side Effect Profile
You may feel uncomfortable answering some of the questions related to how you feel.

Risks to Pregnant Women and Unborn or Nursing Children
The risks of escitalopram during pregnancy is considered low, although there have not been extensive studies. There are no congenital abnormalities known to be associated with escitalopram risk during pregnancy.

If you are pregnant, plan to become pregnant or are breast feeding you **cannot** be in this study. You will be required to use birth control during the study and for 30 days after your last dose of the study drug. Appropriate methods of birth control will be discussed with you. If you are a woman who is able to have children, you will have a pregnancy test to make sure you are not pregnant. Pregnancy tests require a blood or urine sample. You will be told the result of the pregnancy test(s). If you or your partner becomes pregnant during the study, you must tell the

study personnel immediately. We will ask to follow you through your or your partner's pregnancy and the pregnancy outcome.

What happens to the information collected for the research?
If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

Can I stop taking part in this study?
Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study. If you stop taking part in the study you will be asked to return any unused escitalopram and pill diaries you have completed.

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

The study doctor may take you out of the study:

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

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

What are the costs of taking part in this study?
Your involvement in this research study is voluntary and you will not be paid for your participation.

The study agent, escitalopram, will be provided free of charge while you are participating in this study. Neither you nor your insurance provider will be responsible for the costs of any research-only tests or procedures. The blood work for research purposes and the tests on tissue samples taken from your tumor will not be charged to you. It will be paid for by the research study.

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 (i.e., medical history, review of medications, physical exams, performance status, routine blood tests, pregnancy test, x-rays and/or scans for tumor measurement). 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.

Notice for Managed Care (Medicare Advantage Plan) Beneficiaries
Certain services that are required for your care as a participant in a clinical trial can be billed to, and paid by, your medical insurance. These services are referred to as "covered" clinical trial services. However, if you have a Medicare Advantage Plan as part of your medical insurance, this insurance cannot be billed for covered clinical trial services. Instead, traditional Medicare will be billed, and will pay for those services. This has an impact to you. When traditional Medicare pays for such services, you will be responsible for paying the coinsurance amounts applicable to these services, in addition to any other deductibles or co-insurance you may have on your other health coverage. Please speak with a financial counselor to understand what the specific financial impact will be for you associated with participating in this clinical trial.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

What happens if I am injured or hurt because I took part in this study?
If you believe that you are injured as a result of the research procedures being performed, please immediately contact the study doctor.

If injury occurs as a result of your involvement in this research, medical treatment is available from University Hospitals or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

Further information about research-related injuries is available by contacting the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at ([redacted].

What else do I need to know?
Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

HIPAA AUTHORIZATION
Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Jordan Winter, MD and the research study staff at University Hospitals for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition..

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the University Hospitals Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- Case Comprehensive Cancer Center, its study monitors and representatives;
- Other staff from the Principal Investigator's medical practice group;
- Case Comprehensive Cancer Center members and collaborators
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards.

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Consent for Cancer Research

Project Title: CASE6220: A Phase II, Randomized, Double-Blind Trial Comparing Escitalopram to Placebo in Patients with Localized Pancreatic Cancer

Sponsor: Case Comprehensive Cancer Center (Case CCC)

University Hospitals Principal Investigator: Jordan Winter, MD

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Jordan Winter, MD
Case Comprehensive Cancer Center
University Hospitals Cleveland Medical Center
11100 Euclid Ave.
Cleveland, OH 44106

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside University Hospitals cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

University Hospitals will not use your information collected in this study for another research purpose without your written permission; unless the University Hospitals Institutional Review Board assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

Voluntary Participation
Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. De-identified data from this study may be published, presented, or otherwise made publically available. If this happens, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Contact Information

_____ has described to you what is going to be done, the risks, hazards, and benefits involved. The Principal Investigator Jordan Winter can also be contacted at [redacted] If you have any questions, concerns or complaints about the study in the future, you may also contact them later.

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University Hospitals Principal Investigator: Jordan Winter, MD

Emergency or after-hours contact information
If you need to contact study staff outside normal business hours, you may call [redacted] and you will be transferred to the answering service, which can put you in contact with Jordan Winter, MD or the oncologist (cancer doctor) on call.

Where Can I Get More Information?
If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study, research participant's rights; research-related injury; or other human subjects issues, please call the University Hospitals Cleveland Medical Center's Research Subjects Rights Phone line at [redacted] or write to: The Associate Chief Scientific Officer. The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio 44106-7061.

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 Web site at http://cancer.gov/

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

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, if applicable, 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.

Signature
Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have.

A copy of this consent form will be provided to you.

Signature of Participant	Date	Printed Name of Participant

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[USE THIS WHEN A WITNESS IS USED IN THE CONSENTING PROCESS (Common examples include: Inclusion of illiterate individuals, blind individuals or individuals who cannot physically sign but are able to provide informed consent.)]

_____	_____	_____
Signature of Witness	Date	Printed Name of Witness

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____	_____
Signature of Person Obtaining Consent	Date

_____
Printed Name of Person Obtaining Consent