The effect of chemotherapy and stereotactic body radiation therapy for locally advanced, non-resectable pancreatic cancer

NCT02128100

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INFORMED CONSENT AND RESEARCH AUTHORIZATION

The Effect of chemotherapy and Stereotactic Body Radiation Therapy for Locally Advanced, Non-Resectable Pancreatic Cancer

IRB assigned number:	14.0413
NCT #:	NCT02128100
Investigator(s) name & address:	Neal Dunlap, MD James Graham Brown Cancer Center University of Louisville 529 South Jackson Street Louisville, KY 40202
Site(s) where study is to be conducted:	James Graham Brown Cancer Center University of Louisville Hospital

Phone number for subjects to call for questions: 502-562-4360 or 1-888-802-8149 (toll free)

This is a clinical trial, a type of research. Your study doctor will explain the trial to you. Clinical trials include only people who choose to take part. Before you decide whether to take part in this study or not, it is important for you to understand why this clinical trial, or research study, is being done, what it will involve, and how it will affect your daily life. Please take time to read the following information carefully. You may discuss your decision with your friends and family. You can also discuss it with your study doctor. If you have any questions, you can ask your study doctor for more explanation.

Introduction and Background Information

You are invited to participate in this research study because you have pancreatic cancer and will be receiving treatment for it. The study is being conducted at the James Graham Brown Cancer Center and University Hospital under the direction of Neal Dunlap, MD. Approximately 28 local subjects will be invited to participate.

Purpose

The purpose of this study is to find out if chemotherapy combined with Stereotactic Body Radiation Therapy (SBRT) is a safe and effective therapy for the treatment of pancreatic cancer.

SBRT is a radiation therapy that delivers high dose radiation to a target within the body.

Procedures

Your participation in this study will last for approximately 48 months. If you consent to participate, you will have the following procedures while you are in this study.

Screening Period:

Before your treatments begin, certain tests, exams and procedures need to be done to find out if you can be in this clinical research study. If you recently had any of these procedures, they may not have to be repeated. Some of these tests are normally part of regular care and may be done even if you are not part of the study. After all screening procedures are completed, your study doctor will review the results and tell you whether or not you can be included in the study.

- Complete medical history (questions about your health including cancer diagnosis, prior treatments, current medications that you are taking, and allergies you may have).

- Physical examination including body weight, height, and vital signs. (Vital signs will include blood pressure, temperature, breathing rate and heart rate).

- A blood sample (approximately 1 teaspoon [5 mL]) will be collected at screening for biomarker assessments.

- You will be asked to complete a Quality of Life form that will take approximately 8 minutes to finish. You may decline to answer any question that may make you feel uncomfortable.

Treatment planning:

- You will need to have a CT scan with IV contrast. The IV contrast is a liquid dye you will ingest to enhance the scan images. A CT scan, or Computerized tomography, uses several x-rays from different angles to create a 3-
- dimensional (3D) picture of your tumor.

- You will have a 4-dimensional CT scan in order to plan your radiation treatment. This scan is similar to the CT scan with IV contrast but also captures tumor and organ movement. This usually takes about an hour.

- Treatment planning will be performed using either 3D conformal radiotherapy or intensity modulated radiation therapy (IMRT) based on the discretion of the treating physician. IMRT is a type of radiation that allows more accurate targeting of the tumor tissue while avoiding healthy tissue. Standard SBRT treatment will be discussed. Cyberknife treatment may also be used.

Treatment

You and your doctor will decide which type of chemotherapy is recommended for treatment of your cancer. You will receive a total of 8 weeks of chemotherapy prior to any possible radiation therapy. Possible chemotherapy regimens include:

- FOLFIRINOX (a combination of 5-fluorouracil, leucovorin, oxaliplatin, and irinotecan) administered over a total of approximately 6 hours every 2 weeks

- FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) administered over a total of approximately 4 hrs every 2 weeks
- Gemcitabine and nab-Paclitaxel administered over approximately 2 hours weekly for 3 weeks, followed by one rest week.

Following 8 weeks of chemotherapy, you will undergo a CT scan to determine if your cancer has responded to the chemotherapy. If your cancer has progressed or spread at that time, you will not receive radiation as part of this clinical trial, and your doctor will talk to you about other treatment recommendations. If your cancer is stable or has decreased in size, you will then move on to radiation treatments.

- You will have 5 treatments of stereotactic body radiation therapy (SBRT) over the course of two weeks with a minimum of 36 hours in between each treatment.

- A blood sample (approximately 1 teaspoon [5mL]) may be collected for biomarker assessments every two weeks during chemotherapy, again before radiation and then every 6 weeks, 3 months and 6 months after treatment. This blood sample will be collected when you have routine laboratory assessments.

- At screening, 6 weeks post treatment, and at months 3, 6, 9, and 12 post treatment, you will be asked to complete the Quality of Life questionnaire that will take approximately 8 minutes to finish. You may decline to answer any question that may make you feel uncomfortable.

Follow-Up:

- You will have study doctor visits and a CT scan every 3 months during treatment and at 24 months after treatment completion.

- A blood sample (approximately 1 teaspoon [5 mL]) may be collected for biomarker assessments every 3 months, up to and including, 24 months after treatment completion. This blood sample will be collected when you have routine laboratory assessments.

- You will again be asked to fill out the Quality of Life questionnaires at 9 months and 12 months after treatment completion. You do not have to answer any questions that make you feel uncomfortable.

Potential Risks

Chemotherapy Side Effects

The following table details the known side effects related to FOLFIRINOX:

Most Common - More than 5% of Subjects Experienced:
• Neutropenia (decrease in the main part of the white blood cells)

• Febrile neutropenia (development of fever, often with other signs of infection)
• Thrombocytopenia (low platelets in the blood)
• Anemia (low red blood cell count)
• Fatigue (feeling tired)
• Vomiting
• Diarrhea
• Peripheral neuropathy (weakness, numbness and pain, usually in your hands and feet)
• Transaminitis (liver enzymes in the blood stream)
• Thromboembolism (formation of a clot in the blood stream)
• Alopecia (hair loss)
• Stomatitis (mouth sores)
• Hand/foot Syndrome (redness, swelling, and pain on the palms of the hands and/or the soles of the feet. Sometimes blisters appear)
• Abdominal cramping
• Heavy sweating, flushing
• Nerve damage (weakness, numbness and pain, usually in your hands and feet)
• Difficulty swallowing or breathing

The following table details the known side effects related to Gemcitabine and nab-Paclitaxel:

Most Common - More than 5% of Subjects Experienced:
• Leukopenia (reduction of white blood cells in the blood)
• Anemia (low red blood cell count)
• Thrombocytopenia (low platelets in the blood)
• Fatigue (feeling tired)
• Peripheral Neuropathy (weakness, numbness and pain, usually in your hands and feet)
• Diarrhea

Common - 3% of Subjects Experienced:
• Febrile neutropenia (is the development of fever, often with other signs of infection, in a patient with neutropenia, an abnormally low number of neutrophil granulocytes (a type of white blood cell) in the blood)

Radiation Side Effects

Most Common - More than 5% of Subjects Experienced:
• Reversible or permanent hair loss
• Bone marrow toxicity
• Skin pigmentation
• Nausea
• Gastritis (inflammation of the lining of the stomach)

Risks and side effects related to Infusion

The insertion of an intravenous (IV) drip to infuse chemotherapy may cause pain, swelling, bruising, bleeding or (rarely) infection at the place where the needle is inserted. You may also feel dizziness and faint when chemotherapy is being infused.

Risks and side effects related to Radiological Tests

Some of the tests that will be performed (CT scans) will expose you to controlled amounts of radiation. You may feel claustrophobic inside the scanner. The CT scans will involve dyes being injected into one of your veins. There is a risk of allergic reaction to dye. This reaction may be mild (such as a skin rash or hives) to severe (such as breathing difficulties, shock and renal failure). There also is a risk that the injection of dyes or collection of blood samples may cause pain, swelling, bruising, irritation or redness at the site, infection at the site of the needle puncture, or feeling faint. Your study doctor will take steps to prevent this from happening, and may recommend medications that may help with these particular side effects.

Risks of Blood Sample Collection

The collection of blood samples may cause pain, swelling, bruising, irritation or redness at the site, infection at the site of the needle puncture, or feeling faint. Your study doctor will take steps to prevent this from happening and may recommend medications that may help with these particular side effects.

It is very important that you report any side effects to your study doctor as soon as possible; you should not wait until your next scheduled visit.

In addition, you may suffer harms that we have not seen before.

Possible Pregnancy Risks

You should discuss pregnancy risks with your doctor before signing this consent form. Women who are pregnant or breast feeding may not participate in this research study. If you are pregnant or become pregnant, your unborn child may suffer harms that we have not seen before. If you (or your partner) become pregnant while in this study, the sponsor may ask to follow the outcome of the pregnancy. If you agree to allow the study doctor to follow your pregnancy, you will be asked to read and sign a separate consent form for permission to follow the outcome of your pregnancy.

If you are a man taking part in the study and your partner becomes pregnant, the study doctor may ask you to ask your partner for permission to follow her pregnancy. If she agrees, she will be asked to sign a separate consent form mentioned above.

Before starting this research study, females able to have children will have a pregnancy test. Talk to your doctor about the best method of birth control to use while you are in this study. It is important that you call your study doctor at 502-562-4360 right away if you become pregnant or father a child during the course of this study. If you or your partner becomes pregnant, a decision may have to be made whether or not to end the pregnancy.

We do not know the effects of chemotherapy on an unborn baby. There is a risk that your unborn baby could be harmed if you become pregnant during your participation in the study. (If you ask, your study doctor will discuss the possible risks to your unborn child and your options should you become pregnant while in this study.)

Benefits

You may not benefit by participating in this study. The information collected may not benefit you directly; however, the information may be helpful to others.

Alternatives

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

Talk to your study doctor about your choices before you decide if you will take part in this study.

Research Related Injury

If you are injured by being in this research study, the study doctor will arrange for you to get medical treatment. The study site, or your study doctor has not set aside money to pay for treatment of any injury. You and your insurance will be billed for the treatment of these injuries. Before you agree to take part in this research study you should find out whether your insurance will cover an injury in this kind of research. You should talk to the study doctor or staff about this. If you are injured, there is no money set aside for lost wages, discomfort, disability, etc. You do not give up your legal rights by signing this form. If you think you have a research related injury, please call your study doctor, Dr. Dunlap at 502-562-4360.

Compensation
You will not be compensated for your time, inconvenience, or expenses while you are in this study.

Costs

If you are injured by this research, there may be additional costs for participating in this research study. There may be additional costs to you for participating in this research study over the usual costs of your routine care outside of this research study. You and/or your insurance company will be billed for all office visits, tests, medications and procedures involved in this research study and as part

of your routine medical care outside of this research study. Examples include doctor's office visits, blood tests, x-rays, CT scans, EKGs, medications, and hospital stays. You will be responsible for paying your co-pay that is associated with any office visit, test, medication or procedure. None of the charges from the doctor's office, pharmacy or hospital during your participation in this study will be paid for by the study. Some insurance companies will not pay for medical bills for people who participate in a research study. It is your responsibility to find out what costs, if any, your insurance company will cover before taking part in the study. If your insurance company does not pay for your bills associated with this study, you will be responsible for paying them. "According to Kentucky State Law (KRS Chapter 304.17A-136, Coverage for Cancer Clinical Trials) insurance plans may not deny coverage for routine treatment costs incurred during your participation in a cancer study if your insurance plan would have covered those costs had you not been in the study. This law is for your protection. For more information about this law, ask your study doctor.

HIPAA Research Authorization

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) provides federal safeguards for your protected health information (PHI). Examples of PHI are your name, address, and birth date together with your health information. PHI may also include your medical history, results of health exams and lab tests, drugs taken and results of this research study. Your PHI may not be used or shared without your agreement, unless it meets one of the HIPAA exceptions.

State and federal privacy laws protect your health information. In most cases, health information that identifies you can be used or shared by the research team only if you give your permission by signing this form.

If you sign this form your health information will be used and shared to answer the research questions described above and to make sure that the research was done correctly. The time period when information can be used or shared ends when all activities related to this study are completed.

Your access to your health information will not be limited during this study.

You do not have to sign this form. However, if you do not sign this form, you will not be able to take part in this research. This will not change the health care or health care benefits you would otherwise receive.

Site(s) where health information about you will be used or shared for this research:

In our research, the research team will look at and may share information about you and your health. Federal law requires that health care providers and researchers protect the privacy and security of health information that identifies you. We may ask for your health information from the following:

Affiliated Sites:

University of Louisville
University of Louisville Hospital/J. Graham Brown Cancer Center

Protected health information (PHI) that will be used or shared for research

Consultation reports
Diaries and questionnaires
Discharge summaries
Specimens
Healthcare provider orders
History and physical exams
Laboratory, x-ray, and other tests
Records of your operation(s)
Medical progress notes
Records about the study drug and other drugs you may be taking

Revocation of Research Authorization

You may cancel the permission you have given to use and share your protected health information at any time. This means you can tell us to stop using and sharing your protected health information. If you cancel your permission:

- We will stop collecting information about you.
- You may not withdraw information that we had before you told us to stop.
    - We may already have used it or shared it.
    - We may need it to complete the research.
- Staff may ask your permission to follow-up with you if there is a medical reason to do so.

To cancel your permission, you must complete a written "Revocation of Research Authorization" form located at the end of this document. You may also obtain a copy from your study doctor, designated personnel or from the Human Subjects Protections Program Office website (http://louisville.edu/research/humansubjects/subject-information).

Information Available on ClinicalTrials.gov

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Confidentiality

Total privacy cannot be guaranteed. We will protect your privacy to the extent permitted by law. If the results from this study are published, your name will not be made public. Once your information leaves our institution, we cannot promise that others will keep it private.

Your information may be shared with the following:

- The University of Louisville Institutional Review Board, Human Subjects Protection Program Office, Privacy Office and others involved in research administration at the University
- The local research team
- People who are responsible for research and HIPAA oversight at the institutions where the research is conducted
- People responsible for billing, sending and receiving payments related to your participation in the study
- Government agencies, such as:
    - Office for Human Research Protections
    - Office of Civil Rights
    - Food and Drug Administration
- Data Safety Monitoring Board(s) related to the study

Security

Your information will be kept private by password-protected computers and limited access areas for storage of information at University of Louisville premises.

Voluntary Participation

Taking part in this study is completely voluntary. You may choose not to take part at all. If you decide not to be in this study, you won't be penalized or lose any benefits for which you qualify. If you decide to be in this study, you may change your mind and stop taking part at any time. If you decide to stop taking part, you won't be penalized or lose any benefits for which you qualify. You will be told about any new information learned during the study that could affect your decision to continue in the study.

Termination

Your study doctor or the study sponsor has the right to stop this study at any point. Your study doctor may take you out of this study with or without your okay. Reasons why this may occur include:

If you stop taking part in this study, it could harm you. You may be asked to follow these steps for your own safety:

• if your study doctor believes it is in your best interest;
• if you do not follow the study rules; or
• if the study is stopped.

Participation in Other Research Studies

You may take part in this study if you are currently in another non therapeutic research study. It is important to let your doctor know if you are in another research study.

Contact Persons

If you have any questions, concerns, or complaints about the research study, please contact Dr. Neal Dunlap at 502-562-4360.

Research Subject's Rights

If you have any questions about your rights as a research subject, you may call the Human Subjects Protection Program Office at (502) 852-5188. You may discuss any questions about your rights as a research subject, in private, with a member of the Institutional Review Board (IRB). You may also call this number if you have other questions about the research, and you cannot reach the study doctor, or want to talk to someone else. The IRB is an independent committee made up of people from the University community, staff of the institutions, as well as people from the community not connected with these institutions. The IRB has approved the participation of human subjects in this research study.

Concerns and Complaints

If you have concerns or complaints about the research or research staff and you do not wish to give your name, you may call the toll free number 1-877-852-1167. This is a 24 hour hot line answered by people who do not work at the University of Louisville.

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Acknowledgment and Signatures

This informed consent document is not a contract. This document tells you what will happen during the study if you choose to take part. Your signature indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in the study. You are not giving up any legal rights to which you are entitled by signing this informed consent document. You will be given a copy of this consent form to keep for your records.

_____	_____
Subject Name (Please Print)	Signature of Subject Date Signed
_____	_____
Printed Name of Legal Representative (if applicable)	Signature of Legal Representative Date Signed
_____	
Relationship of Legal Representative to Subject	
_____	_____
Printed Name of Person Explaining Consent Form	Signature of Person Explaining Consent Form (if other than the Investigator) Date Signed
_____	_____
Printed Name of Investigator	Signature of Investigator Date Signed

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Principal Investigator:
Neal Dunlap, MD

Phone Numbers:
502-562-4360

Consent version date: April 16, 2018

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REVOCATION OF AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR HEALTH INFORMATION FOR RESEARCH

PI Address: 529 South Jackson Street
Louisville, KY 40202
PI Phone: (502) 562-4360

Return To:

OR

Institutional Review Board
MedCenter One, Suite 200
501 E. Broadway
Louisville, KY 40202

Do not sign this letter unless you are withdrawing from this research. You will be sent confirmation that this notice was received.

To Whom It May Concern:

I would like to discontinue my participation in the research study noted above. I understand that health information already collected will continue to be used as discussed in the Authorization I signed when joining the study.

Your options are (***choose one***):

☐ **Withdraw from Study & Discontinue Authorization:**

Discontinue my authorization for the future use and disclosure of protected health information. In some instances, the research team may need to use your information even after you discontinue your authorization, for example, to notify you or government agencies of any health or safety concerns that were identified as part of your study participation.

☐ **Withdraw from Study, but Continue Authorization:**

Allow the research team to continue collecting information from my personal health information. This would be done only as needed to support the goals of the study and would not be used for purposes other than those already described in the research authorization.

_____ _____
Printed Name and Signature of Subject Date Signed

_____ _____
Signature of Subject's Legal Representative (if subject is unable to sign) Date Signed

_____ _____
Printed Name of Subject's Legal Representative Birthdate of Subject

_____
Relationship of Legal Representative to Subject

_____ _____
Subject's Address Subject's Phone Number

Optional:
I am ending my participation in this study because:

_____