INSTITUTE: National Cancer Institute

STUDY NUMBER: 11-C-0248 PRINCIPAL INVESTIGATOR: Deborah E. Citrin, M.D.

STUDY TITLE: Phase I Trail of ECI301 in Combination with Radiation in Patients with Advanced or Metastatic

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Standard

## INTRODUCTION

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

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

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

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

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

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



### Why is this study being done?

In this study we will be giving an experimental anti-cancer drug, called ECI301, with radiation therapy to patients with metastatic or locally advanced cancer.

ECI301 is an experimental drug that has not yet been studied in humans and is not approved by the U.S. Food and Drug Administration (FDA). Radiation therapy is one way to treat body sites where cancer has spread. In this study, radiation therapy will be given to one or two areas of cancer that are causing pain or might cause an emergency if left untreated. The radiation therapy is not experimental and it is given over two weeks in the standard way that it would be given to those not on a study. The difference between this study and standard treatment is that the experimental drug, ECI301 will be given for two weeks during radiation therapy and for an additional week after radiation therapy. ECI301 is man-made and is similar to a protein residing inside the human body. ECI301 affects a type of white blood cells (effector cells). It is possible that ECI301 will make your cancer more sensitive to radiation therapy. It is also possible that ECI301 will help your body's immune system recognize and destroy the cancer at sites that have not been treated with radiation therapy.

The purpose of this study is to evaluate the potential benefits and side effects of ECI301 when given with radiation therapy. This will help us learn the best dose of ECI301 to give with radiation therapy. In addition, this study will also help us learn how long ECI301 remains in the human body and if ECI301 can change cancers outside of the area treated with radiation therapy.

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

You are being asked to participate because you have either metastatic or locally advanced cancer, and your doctor has determined that you would benefit from radiation therapy.

**How many people will take part in this study?**

A total of up to 30 people will take part in this study.

**Description of Research Study**

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

*Before you begin the study*

All research studies have specific criteria for entry to allow for valid interpretation of the study results and safety of participants, known as eligibility criteria. Before you begin this study you will need to have the following exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care and may be done even if you do not join the study. It is possible that if you recently had some of these tests, they may not need to be repeated.

- History and physical examination, including vital signs (height, weight, blood pressure, heart rate, temperature, breathing rate).
- Standard blood tests to measure: your liver and kidney function, white blood cells, red blood cells and platelets, your blood's ability to clot, your blood sugar and blood electrolytes. If you are a woman who is able to get pregnant, you will also be tested for pregnancy.
- Detailed measurement of your kidney function. This will require you to collect your urine for 24 hours.
- Scans, CT scan, ultrasound, MRI and X-rays of your tumors to measure your disease within 3 weeks of your first dose of ECI301.
- HIV Testing: As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report newly diagnosed HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.
- Hepatitis B and C screening.
- Electrocardiogram to measure your heart function
- Confirmation of diagnosis and stage of disease.

If you meet the eligibility criteria for this study you will be offered the option to participate.

*During the study*

Everyone enrolled in the study will receive the same dose of radiation therapy (3 Gy per daily fraction) Monday through Friday, to a total dose of 30 Gy delivered over two weeks. On this study, one or two sites may be treated. In addition to the radiation therapy, a total of 5 groups of 3-6 patients each will receive increasing doses of ECI301, until we find the highest dose that can be given safely. This is called "dose escalation". Ask your doctor what dose of ECI301 you will be receiving.

Before starting treatment, you will have the option of consenting to a biopsy of the site with that will receive radiation.

During 2, the ECI301 infusion will be given to you in the outpatient clinic or the inpatient unit about one to two hours after your radiation treatment Monday through Friday. Your radiation treatment will be completed at the end of week 2.

At week 3, you will have the option of consenting to a second biopsy of the site that received radiation and a biopsy of another site of cancer that did not receive radiation.

Study Chart

| Day | What to do and what will happen to you |
|---|---|
| Screening/ Baseline | Get routine blood tests; urine tests will be done, including the collection of urine for 24 hours. If you are female you will be tested for pregnancy.<br>Provide a history of how you feel and undergo a physical examination by the research team's Health Care Provider.<br>Research blood and a tumor biopsy (optional).<br>EKG, CT Scan, MRI, x-rays and ultrasound may be done. |
| Week 1 (Monday-Friday) | Provide a history of how you feel and undergo a physical examination by the research team's Health Care Provider.<br>Research blood samples will be taken (Monday).<br>Receive radiation to the sites that your doctor has chosen (Monday-Friday).<br>Report any side effects to the research team. |

| | |
|---|---|
| Week 2<br>(Monday-Friday) | Provide a history of how you feel and undergo a physical examination by the research team's Health Care Provider.<br>Get routine blood tests; urine test will be done (Monday and Friday).<br>Research blood samples will be taken (Monday and Friday).<br>A blood sample will be taken to test the amount of ECI301 in your blood (Monday, Tuesday, Thursday and Friday). On the Monday and Thursday , blood samples will be drawn at 0, 15 and 30 minutes, and 1, 2, 4, 6, 8, and 24 hours after ECI 301 is givenand just before the final dose is given<br>EKG (Monday and Friday)<br>Receive radiation to the sites that your doctor has chosen (Monday-Friday).<br>Receive ECI301 in the vein (IV) in the day hospital approximately 1 to 2 hours after completion of radiation (Monday-Friday).<br>Report any side effects to the research team. |
| Week 3<br>Follow-up | Return to the NIH clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider.<br>Get routine blood tests; urine test will be done.<br>Research blood and a tumor biopsy (optional). |
| Week 4<br>Follow-up | Return to the NIH clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider.<br>Get routine blood tests; urine test will be done.<br>Research blood and a tumor biopsy (optional). |
| Week 6<br>Follow-up | Return to the NIH clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider.<br>Get routine blood tests.<br>Collect urine for 24 hours.<br>CT Scan, MRI, x-rays and ultrasound may be done. |
| Week 12<br>Follow-up | Return to the NIH clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider.<br>Get routine blood tests.<br>CT Scan, MRI, x-rays and ultrasound may be done. |
| 6 months<br>Follow-up | Return to the NIH clinic to see your doctor. Provide a history of how you feel and have a physical exam by your Health Care Provider.<br>Get routine blood tests. |

**Birth Control**

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 6 months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

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

**Alternative Approaches or Treatments**

**What other choices do I have if I do not take part in this study?**
Instead of being in this study, you have these options:

- Getting treatment or care for your cancer without being in a study;
- Taking part in another study;
- 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. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

**Risks or Discomforts of Participation**

**What side effects or risks can I expect from being in this study?**

*ECI301*

You may have side effects while you are taking the study drugs. 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, so it is important to report any changes that you notice, even if your study team does not ask specifically about them. Side effects may be mild or severe. Your study team will give you medicines to help lessen side effects. Many side effects go away with those medicines and others may go away soon after you stop the study drugs. In some cases, side effects can be serious, long lasting, or may never go away. There are no known long-lasting side effects from ECI301. If new information about side effects becomes available, we will make you aware of this new information.

This is the first time that the drug ECI301 has been given to humans. This means that ECI301 has never been tested in humans before this study. The side effects of ECI301 infusions in man are unknown. Studies in animals suggest that ECI301 should be safe at the doses we will use in this protocol.

It is possible that ECI301 will make your cancer more sensitive to radiation therapy. It is also possible that ECI301 will help your body's immune system recognize and destroy the cancer at sites that have not been treated with radiation

therapy. This could result in longer lasting relief of your symptoms or a decrease in the size of your tumor. It is also possible that ECI301 could increase the effects of radiation therapy on normal tissues that are in the treatment area which could result in inflammation (redness or swelling).

The expected discomforts of infusions of ECI301 are the same as those to be expected from other infusions. These include pain and discomfort from a vein being punctured.

*Radiation Therapy*

Some additional side effects may occur with radiation therapy. These side effects are listed below. There may be additional side effects that depend on which parts of your body are being treated. Your doctor will discuss these with you. It is important to let your doctor know if you develop these side effects because changes may need to be made to your treatment. The short-term side effects of radiation tend to go away a few weeks after treatment is completed.

| Likely | Less Likely |
|---|---|
| • Skin irritation in the area radiated<br>• Fatigue<br>• Hair loss in the area treated with radiation | • Decrease in blood counts<br>• Pain in the irradiated area |

*Late Side Effects of Radiation*

Some side effects of radiation can happen many months or years after treatment. It is impossible to predict who will develop long-term side effects. Your doctor will discuss these risks with you.

**Potential Benefits of Participation**

**Are there benefits to taking part in this study?**

The aim of this study is to see if this experimental treatment will cause your cancer to shrink. We hope that you will get personal medical benefit from taking part in this study, but we cannot be certain. These potential benefits could include shrinking your cancer or decreasing your symptoms, such as pain, that are caused by the cancer. Because there is not much information about ECI301's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

**Research Subject's Rights**

**What are the costs of taking part in this study?**

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

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs even if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.

- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

**Stopping Therapy**

Your doctor may decide to stop your therapy for the following reasons:
- if he/she believes that it is in your best interest
- if your disease gets worse during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

If this happens, you will be informed of the reason therapy is being stopped.

You can choose to stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to both the study doctor and your regular doctor first.

**Conflict of Interest**

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details on this process *http://ethics.od.nih.gov/procedures/COI-Protocol-Review-Guide.pdf*. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

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

**Optional Biopsies**

A core tumor biopsy uses a hollow needle to extract tissue from the tumor. The most common side effect of a core tumor biopsy is pain. Other rare complications include: bleeding, which in rare cases may be severe enough to require a transfusion; puncturing a nearby organ; or very rarely (less than 1%) death.

Optional core tumor biopsies will be taken before treatment and again one week after finishing radiation. These biopsies will be taken from the target lesion (the site that is being radiated) before treatment and from both the target lesion and a separate un-irradiated lesion (a site that was not irradiated) at the one week follow up time point. Biopsies will be performed in collaboration with interventional radiology. Standard techniques will be used for needle biopsies which may include CT and/or ultrasound-guided biopsy. In some cases, such biopsies may be done quickly and helped by the use of navigation tools, such as a laser guide or GPS-electromagnetic tracking of the needle or ultrasound, to determine which exact angle the biopsy needle will be inserted.

The biopsies to be performed are exclusively for research purposes and will not benefit you. It might help other people in the future. Even if you sign "yes" to have the biopsy you can change your mind at any time. Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. The decision to participate in this part of the research is optional, and no matter what you decide to do, it will not affect your care.

I agree to have the tumor biopsies for the research tests in this study.

Yes No Initials_____

**Optional Studies**

We would like to keep some of the tissue and blood that are collected for future research. These specimens will be identified by a number and not your name. Your specimens will be used for research purposes only and will not benefit you. It is also possible that the stored specimens may never be used. Results of research done on your specimens will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you decide now that your tissue and blood can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue, blood, and urine. Then any tissue and blood that remain will be destroyed.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

**1.** My tissue and blood specimens may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Initials_____

**2**. My specimens may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials_____

**3**. Someone may contact me in the future to ask permission to use my specimen(s) in new research not included in this consent.

Yes No Initials_____

## OTHER PERTINENT INFORMATION

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

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

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

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

**4. Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Deborah Citrin, M.D., Building 10, Room CRC B2-3500, Telephone: 301-496-5457. You may also call the Clinical Center Patient Representative at (301) 496-2626. If you have any questions about the use of your tissue for future research studies, you may also contact the Office of the Clinical Director, Telephone: 301-496-4251.

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

**COMPLETE APPROPRIATE ITEM(S) BELOW:**

**A. Adult Patient's Consent**

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

Signature of Adult Patient/Legal Representative _____ Date _____

Print Name _____

**B. Parent's Permission for Minor Patient.**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian _____ Date _____

Print Name _____

**C. Child's Verbal Assent (If Applicable)**

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

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

**THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JULY 11, 2011 THROUGH JULY 10, 2012.**

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____