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CONSENT TO TAKE PART IN A RESEARCH STUDY

Title of Study: **A Pilot Study of Neoadjuvant Cetuximab in Advanced Squamous Cell Carcinomas of Skin (SCCS)**

Principal Investigator: **Janice Mehnert, M.D.**
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This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

The study doctor, Dr. Janice Mehnert, or another member of the study team (an investigator) will also be asked to sign this informed consent form. You will be given a copy of the signed consent form to keep.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Sponsor of the study:
The Rutgers Cancer Institute of New Jersey is the sponsor of this research study. The costs that are usually covered include things such as research laboratory tests required by the study, and the costs of collecting all of the information required by the study.

Why is this study being done?
This study is being done to test whether a drug called cetuximab will help shrink large skin tumors called squamous cell carcinomas. In other words, because your tumor may be large or may be penetrating other tissues beneath the skin such as muscle or bone, treating the tumor now with surgery may be difficult and dangerous. This study will test whether giving you the drug called cetuximab may help to shrink the tumor to a small enough size so that the surgeon can remove it and increase the chances of a less extensive surgery.

Cetuximab is a drug that attacks a part of the skin called the EGFR receptor. Many squamous skin cancers have this receptor. This receptor is also present in many tumors that develop after uv-light or sun exposure of the skin. There are reports of antitumor activity of cetuximab in advanced cases of squamous carcinoma of the skin.

We plan to measure how the tumor responds to cetuximab by measuring the size and the time it takes for the tumor to shrink. We also want to determine whether cetuximab will improve the amount of surgical resection necessary.

The primary theory is that cetuximab used before surgery for squamous cell carcinomas is both safe and well tolerated and that its use may help the treatment of advanced cases of Squamous Cell Carcinomas when used before surgery.
We hope to treat unresectable (a tumor that cannot be completely removed by surgery) squamous cell carcinomas with 8 weeks of the use of cetuximab, and monitor patients for disease response, adverse events (unexpected side-effects), and overall safety. Potentially, patients may be able to go on to surgery if adequate disease response is achieved. The hope is that the results from this study will lead to a larger clinical trial testing the effectiveness of this treatment for this disease.

We also want to compare any change in the genes of the tumor or mutations, that may help identify those tumors that respond to cetuximab the best. Your tumor, skin, and blood will be analyzed for indications that may predict response or resistance to cetuximab therapy. The goal of these studies is to learn which patients may benefit from this approach in order to better the process of selecting patients for cetuximab therapy.

Why have you been asked to take part in this study?
You have been asked to take part in this study because you have untreated or relapsed squamous cell carcinoma of the skin that is considered to be aggressive and locally advanced as determined by any of the following criteria:

a) The tumor's size is 2 cm or more,
b) The tumor is invading deep tissues such as muscle, cartilage or bone;
c) The tumor is growing into the nerves and/or
d) The tumor has traveled (metastasized) to the lymph nodes.

Your doctor will help you understand which one of the above categories describes your medical situation.

Who may take part in this study? And who may not?
You may be included in this study if

- You are healthy enough to tolerate the treatment
- Have untreated or relapsed SCCS (Squamous Cell Carcinomas of Skin) that is considered to be aggressive and locally advanced
- You agree to be treated with cetuximab prior to surgery

You may not be included in this study if

- You are less than 18 years of age
- Have any other active cancer in certain situations. For example, patients who have second cancers or cancers that do not require active treatment, or patients whose second cancers are treated and disease free for at least 3 years may be eligible. As well as patient with in situ carcinoma (such as in situ carcinoma of the cervix) or, additional skin cancers that have been definitively treated by surgery and/or radiation may be eligible. If you have a second cancer, please discuss this with your treating physician.
- Have any conditions that would interfere with your safety if you participated in this study
- Are, or intend to become, pregnant

The study doctor and/or research team will also ask you other questions about your medical history in order to make sure you qualify to be in this study.

How long will the study take and how many subjects will participate?

You will be on study for the 8 weeks of active cetuximab treatment followed by assessment of disease response and determination of whether the lesion is potentially resectable.

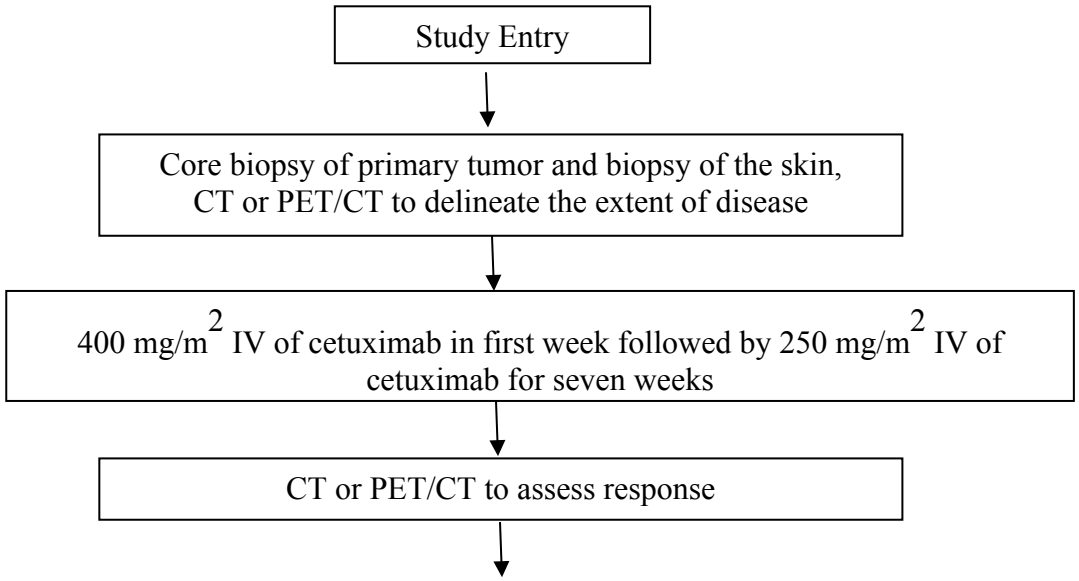
This is the length of time for initial biopsy, treatment with cetuximab, and repeat biopsy or surgery or radiation. You will also have follow up on study for a period of 2 years.

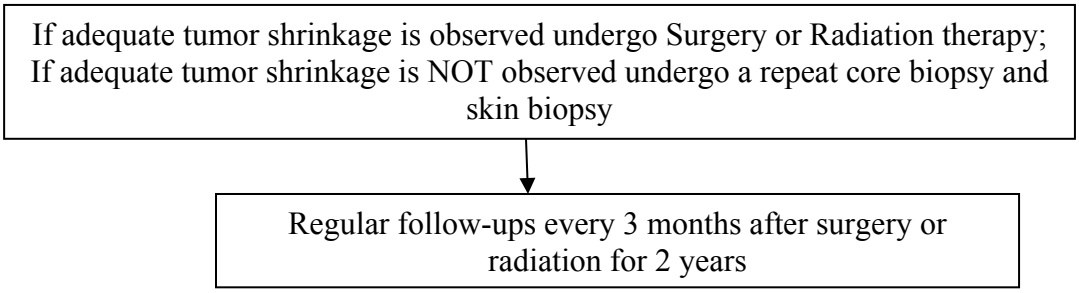
Keep in mind that after the initial treatment with cetuximab, the follow up procedures (including follow up scans and examinations) are similar to what you would undergo even if not participating in a study.

This study will take roughly 2 years to accrue and another 2 years for follow up. Approximately 20 subjects will take part in the study from the Rutgers Cancer Institute of New Jersey and CINJ Oncology Group.

What will you be asked to do if you take part in this research study?

This is a diagram of the study:





Before you are started on treatment, many tests will be performed to see if you can enroll in this study. While on treatment, many tests will be performed to see how you are tolerating treatment. Many of these tests would be performed even if you were receiving standard treatment. Tests that have an asterisk (*) next to them are the tests that are being performed specifically as part of this study

Before starting treatment

- Sign this informed consent
- History and physical
- Blood test
  - Complete blood count (CBC)
  - Chemistry tests
  - Collection of blood for studies of biologic markers
- Pregnancy test (if you are a woman able to have children)
- PET/CT, CT neck, chest/abdomen and pelvis or MRI of neck (special tests that look at the organs in your body)
- Baseline Incisional/core biopsy of primary tumor and loco-regional lymph nodes if involved and skin biopsy
- Photo of tumor and/or rash at head, neck, upper torso. The pictures taken of your skin cancers will be taken so that they do not identify you. If you agree to allow pictures to be taken of your skin, any health data that identifies you will be kept confidential.

During treatment

- You will be treated in two 4 week cycles. One cycle is 4 weeks of treatment
- You will be given cetuximab intravenously (through the vein) once every week for a total of 8 weeks.
- History and physical
  - Once every 4 weeks before treatment
- Evaluation of side effects
  - Weekly
- Photo of tumor and/or rash at head, neck, upper torso
  - Weekly
- Blood test
  - CBC will be done weekly, chemistry once every 4 weeks

- PET/CT, CT neck, chest/abdomen and pelvis or MRI of neck
    - During week 9 after completing 8 weeks of cetuximab treatment
    - Repeat tumor biopsy*: *If you are not going to have surgery a biopsy will be done again before starting any new treatment or any radiation therapy.*
    - Incisional/core biopsy of primary tumor and loco-regional lymph nodes if involved and skin biopsy
- Surgery after treatment with cetuximab is completed if deemed appropriate by the doctors. Some of the tumor and skin removed from surgery will be tested.
- If no surgery is indicated you may undergo radiation therapy or other types of treatment.
- If the tumor comes back or starts growing during treatment or a new tumor starts to grow at a new site, another biopsy will be done.

After completing treatment: 30 days after surgery or completing radiation you will return to the doctor's office for the following assessments and then you will undergo follow up every three months for up to 2 years:

- History and physical, including evaluation of side effects
- Blood test (CBC, chemistry, tests to measure how your blood clots)
- PET/CT, CT neck, chest/abdomen and pelvis or MRI of neck (every three months following conclusion of surgery or radiation therapy)

Women of Childbearing Age

Women of childbearing age must agree to undergo a pregnancy test prior to therapy and to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study participation and for 6 months after. Should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her treating physician immediately.

What are the risks and/or discomforts you might experience if you take part in this study?
Most of the risks and discomforts are standard when receiving cetuximab regardless of whether you are on protocol or not. Some of these side effects include, in the short term:

- *Common Side Effects:*
    - *Skin rash: it is believed that if you get a skin rash while on cetuximab the tumor will get smaller or respond to further therapy. The skin rash has raised lesions and looks like acne. It can happen in any part of the skin including the face. This side effect is common and occurs in about 76-88% of patients.*
        - *The skin rash may also cause the skin to peel off, like after a burn*
        - *Nails may change color*
        - *Eyes may get itchy*
    - *You will need to limit your exposure to sun*
        - *Photosensitivity:*

- *Skin rash or discoloration that may be painful with exposure to sun*

- *Rare but Serious Reactions:*
  - *Allergic reactions: you may be allergic to the medication and an asthma type of attack may happen while receiving the medication. Also the blood pressure may drop and chest pain may occur. When this happens the doctors will stop the infusion and give you medication for allergic reactions. Depending on the doctors evaluation you may be given the drug but at a slower pace.*
    - *A very serious drug reaction called anaphylaxis may occur and this can be life threatening. If this happens there will be no further cetuximab therapy*
  - *Skin infections may occur and can be serious.*
    - *Lung reactions: these reactions are rare but serious*
    - *Less serious reactions are called electrolyte imbalances. The level of Magnesium, potassium and calcium in the blood may be lowered. Your doctor will supplement you with these electrolytes if necessary. The doctor will also monitor your electrolyte levels up to 28 weeks after discontinuation of cetuximab.*

Risks associated with the biopsy:

There may be some temporary pain or discomfort associated with the biopsy procedure. After the biopsy procedure(s), there may be slight pain, redness, swelling, bleeding, bruising, and/or drainage at the site that usually goes away in a few days. Rarely, abnormal wound healing, fever, infection, or allergic reaction to the numbing medicine may happen. Your doctor will give you a separate consent form for this procedure. This is done with a local anesthetic and may require a stitch to close the skin.

Are there any benefits for you if you choose to take part in this research study?
The main benefit is that this is a form of treatment for your squamous cell carcinomas of skin that could promote improved outcomes for yourself and others with this disease. If you respond to cetuximab, then you undergo surgery or radiation; with the hope of less toxicity than if you received standard therapy. The other benefit is indirect, in that information derived from your biopsies will be analyzed, and may contribute to understanding of this disease and why some cancers are more resistant to cetuximab than others.

What are your alternatives if you don't want to take part in this study?
Talk to your doctor about your choices before you decide if you will take part in this study. You are under no obligation to take part in this research study. If you decide that you do not wish to take part in this study, you are free to leave the study at any time. Your other choices may include:,

- ***Receiving surgical resection and/or radiation, or no treatment for your cancer at all if you decline these.***

How will you know if new information is learned that may affect whether you are willing to stay in this research study?

During the course of the study, you will be updated about any new information that may affect whether you are willing to go on taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will there be any cost to you to take part in this study?
You and/or your insurance company will be billed for the costs of your treatment that are considered standard of care (for example, cetu
ximab, doctor/ Advanced Practice Nurse (APN) visits, nursing care to administer the treatments, routine lab tests, restaging scans, etc.) as you would have received these services even if you were not participating in this study. You will be responsible for any co-payments due for office visits, co-insurances and deductibles due on any tests and/or procedures that are required and considered standard care.

If you have any questions about insurance coverage, including any out of pocket expenses you might incur, or which laboratory or facilities you are allowed to have tests at, a financial counselor will be made available to you upon request.

Optional and/or research related items such as tumor tissue collection and blood samples will be paid for by the Cancer Institute of New Jersey.

Will you be paid to take part in this study?
You will not be paid to take part in this study.

How will information about you be kept private or confidential?
All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed.

Your personal health information, identifiers and research data are stored and kept in a secure area in the Rutgers Cancer Institute of New Jersey. Computer screens containing personal health identifiers are inaccessible to public view. Only the study doctor and research team including Tissue Bio-repository team at Rutgers Cancer Institute of New Jersey (where your samples will be kept) will have direct access.

What will happen if you are injured during this study?
If you take part in this study, you will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment.

In addition, it is possible that during the course of this study, new adverse effects of the study drug(s) that result in personal injury may be discovered. Please refer to section “what are the risks and/or discomforts you might experience if you take part in this study?”

The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g.,

Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. The University will provide no financial compensation and no other type of assistance is available from the University.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?
Participation in this study is voluntary. You may choose not to participate or you may change your mind at any time.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

You may also withdraw your consent for the use of your data, but you must do this in writing to Dr. Janice Mehnert (address provided on page 1).

Any data that has already been sent to the Cancer Institute and/or the Office of Human Research Services at the Rutgers Cancer Institute of New Jersey cannot be withdrawn because there may not be any identifiers to link the data with you. The Food and Drug Administration require us however, to continue to report anything that relates to the safety of these drugs.

At any time, the study doctor can take you out of this study because it would not be in your best interest to stay in it. Your study doctor can stop treatment even if you are willing to stay in the study.

If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can you call if you have any questions?
If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study doctor:
Janice Mehnert, M.D.
The Cancer Institute of New Jersey
(732) 235-8675

If you have any questions about your rights as a research subject, you can call:

IRB Director
(732)-235-9806

What are your rights if you decide to take part in this research study?
You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

Protected Health information

Protected Health Information (PHI) under HIPAA means any information that identifies an individual and relates to at least one of the following:

- The individual's past, present or future physical or mental health
- The provision of health care to the individual
- The past, present or future payment for health care

The next few paragraphs tell you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization (permission) and informed consent form as required or allowed by law. Because we are committed to protecting your health information, some of the paragraphs that follow repeat what we described to you earlier in this consent form about what information we will collect about you, how we will use it, when or if it will be shared with others, and the measures we will take to protect your privacy and the confidentiality of your personal information.

Please read this authorization section and the consent form carefully. Ask questions if anything is not understandable to you.

Authorization to use your health information for research purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

Do you have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study and receive any research related products. However, signing the form is not a condition for receiving any medical care outside the study.

If you sign, can you revoke your authorization or withdraw your information later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows the researchers to continue using and disclosing your information. Therefore, you should be aware that the researchers might continue to use and disclose the health information that was provided before you withdrew your authorization if necessary to maintain integrity of the research or if the data had already been stripped of all identifiers.

If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you may do so in writing by contacting Dr Janice Mehnert in writing.

What personal information will be used or disclosed?

Your health information related to this study may be used or disclosed in connection with this research study, including, but not limited to, information in your medical record such as certain information indicating or relating to a particular medical condition, blood and other tissue samples and related records, physical examinations, x-rays, MRI's, etc. Your personal identity, that is your name, address, and other identifiers, will be kept confidential. You will have a code number and your actual name will not be used. Only your study doctor will be able to link the code number to your name.
Your data may be used in scientific publications. If the findings from the study are published, you will not be identified by name. Your identity will be kept confidential. The exception to this rule will be when there is a court order or when a law exists requiring the study doctor to report communicable diseases. In this case, you will be informed of the intent to disclose this information to the state agency. Such a law exists in New Jersey for diseases such as cancer, infectious diseases such as hepatitis, HIV, viruses and many others.

The Cancer Institute will be allowed to examine the data in order to analyze the information obtained from this study, and for general health research.

In applications for marketing authorization your data may be submitted to domestic and foreign drug regulatory agencies.

Your data may also be sent to domestic and foreign drug regulatory agencies if you should suffer a bad reaction to the study drug.

Who may use or disclose the information?
The following parties are authorized to use and/or disclose your health information in connection with this research study:

- Rutgers University Institutional Review Board (IRB - a committee that reviews research studies to protect people participating in research.)
- Rutgers University
- Robert Wood Johnson University Hospital (RWJUH)
- Rutgers Cancer Institute of New Jersey

Who may receive/use the information?
The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- U.S. Food and Drug Administration (FDA)
- The Office for Human Research Protections (OHRP) in the U.S. Department of Health and Human Services (DHHS)

Your information may be re-disclosed (shared) by the recipients described above, if they are not required by law to protect the privacy of the information.

When will your authorization expire?

There is no set date at which your authorization will expire. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

Will access to your medical record be limited during the study?
To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it were used to make medical or billing decisions about you and was included in your official medical record.

Where can you get more information?
You may call the National Cancer Institute's Cancer Information Service at:
Voice: 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/

If you do not have access to a personal computer, you may access these websites and other information at a computer in the Resource and Learning Center on the second floor of the Rutgers Cancer Institute of New Jersey at no cost to you.

AGREEMENT TO PARTICIPATE
I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

I agree to take part in this study.

Subject Name:_____

Subject Signature:_____ Date:_____

FOR NON-ENGLISH SPEAKING SUBJECTS:

Signature of Reader/Translator If the Subject Does Not Read English Well:

The person who has signed above, _____, does not read English well. You read English well and are fluent in _____ (*name of the language)*, a language that the subject (his/her parent(s)/legal guardian) understands well. You understand the content of this consent form and you have translated for the subject (his/her parent(s)/legal guardian) the entire content of this form. To the best of your knowledge, the subject (his/her parent(s)/legal guardian) understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered

(his/her parent(s)/legal guardian).

Reader/Translator Name:_____

Reader/Translator Signature:_____ Date:_____

Witness Name:_____

Witness Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:
To the best of your ability, you have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legal guardian have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____