Consent to Participate in Research

Study Title: A Randomized, Phase II Study of Ficlatuzumab with or without Cetuximab in Patients with Cetuximab-Resistant, Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Principal Investigator: Julie E. Bauman, MD, MPH

Sponsor: University of Arizona Cancer Center

This is a consent form for research participation. It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.

This is a clinical trial, a type of research study. Clinical trials include only people who choose to take part. You are being asked to take part in this study because you have Head and Neck Squamous Cell Carcinoma. This study will enroll both males and females, 18 years of age or older, for whom cetuximab did not or does not work. Your doctor will determine your ability and eligibility to participate in this study.

Taking part in this study is entirely voluntary and up to you to decide. In order to decide whether or not you wish to take part, you should understand enough about its purpose, procedure, risks, benefits, and costs to make an informed decision. This process is known as Informed Consent.

Before you agree to participate in this study, it is important for you to understand why the study is being done and what the requirements are for your participation. Please take time to read the following information carefully and ask questions if anything is not clear. This consent form describes the purpose, procedures, precautions, the possible benefits, risks (side effects), and discomforts that go along with your participation in this study. This consent form also outlines your rights as a subject involved in a study. If you agree to participate, you will be asked to sign this form.

The consent form also describes the alternative procedures that are available to you, and your right to withdraw from the study at any time. Take as much time as you want to decide whether or not you wish to take part.

The University receives compensation from the sponsor of this study for the conduct of this study. If you have any questions, please discuss this with your study doctor.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by US 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.

Why is this study being done?

The main goal of this research study is to study the safety and effectiveness of ficlatuzumab with or without cetuximab to determine which will be more effective, as well as to learn the potential side effects of ficlatuzumab alone or in combination with cetuximab.

It was recently determined that not enough patients were benefiting from receiving only ficlatuzumab. Although some patients benefited, there were not enough to continue adding patients to that group. Therefore, if you are eligible for the study, you will receive ficlatuzumab with cetuximab.

Ficlatuzumab is considered an "experimental" drug because it has not been approved for commercial use in the treatment of cancer by any authority that regulates new drugs, including the U.S. Food and Drug Administration (FDA). Ficlatuzumab is a monoclonal antibody, also referred to as a targeted therapy or an immunotherapy. Ficlatuzumab works by blocking growth signals that let a cancer cell survive and reproduce, and may also help the immune system recognize and fight cancer.

Cetuximab is an approved chemotherapy drug by the Federal Drug Administration (FDA) for treating squamous cell carcinoma of the head and neck in which prior platinum-based therapy (chemotherapy) has failed. Cetuximab is a monoclonal antibody, also referred to as a targeted therapy or an immunotherapy. Cetuximab is given as an anti-cancer therapy because it blocks growth signals that lets a cancer cell survive and reproduce, and helps the immune system recognize and fight cancer.

If you participate in this study we will also collect samples of blood and tissue to determine how your body processes the study drug combination of cetuximab and ficlatuzumab and the effects they have on the various biomarkers (a DNA sequence that causes disease or is associated with susceptibility to disease) related to your cancer.

What will happen if I take part in this study?
If you join this study, you will be asked to sign this consent form before you receive any study related tests or procedures.

Screening Procedures
After signing this consent form, you will need to have exams, tests or procedures to find out if you can be in the study. Some exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study, such as medical history, review of your current medications, routine blood draws, and physical examination. If you have had some of them recently, within 28 days of the first dose of study drugs, they may not need to be repeated. This will be up to your study doctor. Some procedures may be done only for the purposes of the research. This includes a blood draw and a pregnancy test if applicable. The tests will be done by your study doctor, or a nurse, physician assistant, nurse practitioner, or laboratory technician under your study doctor's supervision, and will take about 2-4 hours to complete. If the results of these screening tests determine you are not eligible, you will be removed from the study and your doctor will discuss alternative treatments with you.

Baseline Research Procedures
After the screening procedures, if it is determined you are eligible to participate, you will undergo additional procedures that are only being performed because you have agreed to participate in this study. These will be referred to as research procedures and are described below. These will be done by your study doctor, a nurse, physician assistant, nurse practitioner, phlebotomist, pharmacist, or laboratory technician under your study doctor's supervision and will take about 3-4 hours to complete.

- **Blood draw** (about 5 Tablespoons) for various research blood tests may be performed after consent and before first study treatment. This and all research blood may be drawn at the same time blood is drawn for your regular care.
- **Research Biopsy:** You will also have a biopsy prior to the first study treatment so long as it is safe and/or feasible. This will be used for research testing only.
    - To be in the study, you must agree to have the research biopsy performed. A biopsy is a standard, commonly performed procedure in which a piece of tissue

(tumor or mass) is taken and studied under the microscope. Details on the biopsy procedure are provided at the end of this document.

- **Quality of life assessment:** The Functional Assessment of Cancer Therapy-Head and Neck (FACT H&N) Symptom Index Questionnaire will be completed to assess your symptoms related to your cancer. This may be performed any time after consent but prior to your first study treatment and takes about 5 minutes to complete. If any questions make you feel uncomfortable, you may skip those questions and not give an answer. This can be done during an in-person visit but can also be done by phone, or other method, if needed.
    - The questionnaire asks about your view of how your life has been affected by cancer and its treatment. There are 10 questions. This information will help doctors better understand how patients feel during treatments and what effects the medicines are having.
- **Tobacco Use Assessment:** A questionnaire about your tobacco use history will be completed. This takes about 5-10 minutes to complete. This can be done during an in-person visit but can also be done by phone, or other method, if needed.
    - The assessment has 13 questions about the type of tobacco and quantity you may have used. If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

Archival tumor tissue (tissue from a prior biopsy or tumor excision) will be requested to be used for research purposes to learn more about the makeup of tumor tissues and the development of cancer.

If you are eligible to receive the study drug(s), you will receive ficlatuzumab in combination with cetuximab.

Study procedures will occur on a regular schedule, known as a “cycle.” Each cycle is 4 weeks.

Study Drug Administration

You will receive the study drugs every 2 weeks. You will be evaluated periodically to determine if the study treatment is working. If it is, you will continue at the same dose and schedule for as long as the study treatment helps or until March 31, 2021, whichever is sooner. (See the section below titled, How long will I be in this study?)

- You will receive the study drugs on the same day.
- The drugs will be administered intravenously (through the vein). You will receive cetuximab first, and then ficlatuzumab.
- Before you receive cetuximab, you will receive pre-medications to prevent allergic reactions and to replace body fluids, if necessary.
- You will receive cetuximab. The cetuximab infusion will last between 1 to 2 hours.
- There will be 30-60 minutes between the cetuximab and ficlatuzumab infusions.
- You will then receive ficlatuzumab. The ficlatuzumab infusion will last between 30 to 60 minutes.

- The infusions will take about 4 hours total, including administration of pre-medications.

Study Drug Doses

- Ficlatuzumab will be administered at the dose of 20 mg/kg IV every 2 weeks (+/- 3 days).
- Cetuximab will be administered at the dose of 500 mg/m^2 IV every 2 weeks (+/- 3 days).
- Dose modifications for ficlatuzumab and cetuximab are allowed if you experience certain side effects from the study medications.

Every Two Weeks

(The following may be performed on the day of or within the 3 days prior to the study drug infusion)

- Toxicity/adverse event assessment to evaluate if the study drugs are having harmful effects on you. Note: if a toxicity occurs, this will be assessed at each visit and you may need to be seen more frequently until the issue is resolved.
- Physical examination, including vital signs, weight and performance status
- Update of concomitant medications
- Blood draw (about 5 tablespoons) research purposes

Every 8 Weeks (The end of even cycles)

(The following may be performed on the day of or within the 3 days prior to the study drug infusion)

- As part of your regular care, you will have a tumor assessment every 8 weeks (+/- 7 days). Information from this procedure, which is typically a CT Scan or MRI, will be used to assess your response to the study drug(s).
- Quality of life assessment (FACT-H&N) – end of cycle 2 and cycle 6 only.
    - This questionnaire can be done by phone or mail, or other method, as needed.
- Toxicity/adverse event assessment to evaluate if the study drug/study drugs are having harmful effects on you. Note: if a toxicity occurs, this will be assessed at each study visit and you may need to be seen more frequently until the issue is resolved.
- Blood draw (about 5 tablespoons) for research purposes

Typically, visits when you receive the study drug infusion will take about 4-5 hours. Visits may take longer depending on how long it takes to prepare the study drug(s) for infusion. It is possible that that visits could take 5-8 hours.

If you miss an in-person visit, the study staff may contact you by phone or other method to obtain an update and assess your health to the extent possible. If you have telemedicine visits for your regular care, this information can be obtained during those visits.

End of Treatment Evaluation:

When you discontinue study treatment for any reason you will have an end-of-treatment visit within 30 days and the following tests will be done, if possible, unless performed within the previous 2 weeks:

- Toxicity/adverse event assessment to evaluate if the study drugs are having harmful effects on you. Note: if a toxicity occurs, you may need to be seen about every 2 weeks until the issue is resolved.
- Blood samples (about 5 tablespoons) for research purposes.
- The Quality of Life assessment if you end the study treatment at Cycle 2 or Cycle 6.

End of Treatment Evaluations if Ending Treatment Due to the Study Drug Expiration:
The latest that ficlatuzumab will be available is March 31, 2021. If you are continuing the study treatment into March 2021, your study doctor will discuss the transition with you ahead of time to determine continuation of treatment for your cancer.

At that time, you will stop receiving the study drug, but your participation in the study will not end. You will have an end-of-treatment visit as described above. You may be asked to complete the quality of life assessment questionnaire if you are stopping the study treatment before the end of Cycle 6. You will be followed for any new adverse events or pregnancy for 60 days. Then you will enter the follow-up portion of the study. You will be followed every 3 months to determine your survival status.

Long-Term Follow up:

- You will be followed for 60 days after the last dose of study drug for any new adverse events, and for pregnancy, if applicable. This may include a phone call to assess adverse events, or you may be assessed during a visit for your regular care.
- Any toxicities/adverse events will be followed until they resolve or stabilize.
- If you stopped the study treatment for due to disease progression, or due to the study drug expiration, you will be followed about every 3 months to determine your survival status.
- If you stopped the study treatment for a reason other than disease progression, you will be followed about every 8 weeks to determine your survival and disease status.
    - If you experience disease progression during the follow-up period:
        - A blood draw (about 5 tablespoons) for research purposes will be performed.
        - You will then be followed every 3 months for 2 years to determine your survival status.

The study procedures may overlap with your regular cancer care. Information from your regular care will be collected for the study. This includes physical exams, vital signs, and regular lab tests. Only procedures done for the research are listed above. There is a possibility that the tests or procedures may need to be done at times other than those listed above. These may be done if your doctor determines they are medically necessary to monitor your illness or any side effects you may be experiencing. It is important that you call your doctor if at any time you are experiencing side effects you cannot tolerate.

How long will I be in this study?
It is unknown how long you will be in the study. The screening evaluation will take place within the 4 weeks prior to the first study treatment. You will continue the study treatment if it is working to shrink or stabilize your cancer or until March 31, 2021. The last ficlatuzumab infusions will be on or before March 31, 2021. Ficlatuzumab will not be available after that date because the study drug is expiring.

Follow-up will begin when you stop the study treatment. If you experience disease progression, either during the study treatment or while in follow up, or if you stop the study treatment due to the study drug expiration you will then be followed for survival every 3 months for two years.

How many people will take part in this study?
Up to 74 people will participate in this research study at all sites. Locally, we expect to enroll about 22 people in this research study.

What benefits can I expect from being in this study?
We cannot predict in advance whether you will receive any direct benefit from participating in this study or not. Taking part in this study may or may not make your health better. A possible benefit of your participation may be that researchers may learn more about your disease, which may, in turn, help others.

What risks, side effects or discomforts can I expect from being in the study?
Drugs for cancer are strong and have side effects. You may have side effects while on the study. As with any experimental procedure, there may be adverse events or side effects that are currently unknown. Side effects can go away shortly after drug administration is stopped, but some risks could be long-lasting, permanent, serious, life threatening, or even cause death. Everyone taking part in the study will be watched carefully for any side effects. Your doctor may also give you additional medications to ease any side effects you may experience during the study. You should talk to your study doctor about these medications and any side effects you may experience while taking part in the study.

Ficlatuzumab Risks
Because Ficlatuzumab is an investigational drug, there may be other risks that are unknown at this time. The following are the most commonly indicated as related to treatment in previous clinical studies:

Side effects of Ficlatuzumab (occurring in 5% of participants or more)
- Decreased appetite
- Diarrhea
- Swelling of the feet, ankles or other parts of the body
- Nausea
- Rash, or an appearance similar to acne
- Bacterial skin infection, which may cause swelling, redness, and sensitivity
- Vomiting

Side effects of Ficlatuzumab (occurring in 5% of participants or less)
- Dry skin
- Feeling weak or tired
- Headache
- Electrolytes, such as potassium, magnesium, etc., may decrease (the most common symptoms of this are muscle tremor, weakness, confusion, irregular heartbeat)
- Low albumin in the blood (symptoms can include swelling of the feet or ankles)
- Low red blood cells (anemia)
- Muscle pain or tenderness
- Itchiness
- Chills
- Dizziness
- Muscle Spasms
- Infection in the blood
- Pneumonitis (lung inflammation) which can cause difficulty breathing

One participant experienced a mild infusion-related reaction (e.g. chills, shaking, and fever) related to ficlatuzumab. The reaction was treated and resolved the same day. Approximately 4 weeks later, the participant had a second mild infusion-related reaction to ficlatuzumab. The second reaction was treated and resolved the same day. No further infusion-related reactions were reported.

This study uses the combination of ficlatuzumab and cetuximab. The risks for the combination of these drugs are currently unknown. Below please find details the risks of cetuximab alone.

The following two risks have been found when ficlatuzumab is taken in combination with the same kind of medication as cetuximab. These are also risks of cetuximab alone.

- Inflammation of the skin around your finger and toe nails
- Bleeding gums

Cetuximab (Erbitux®) Risks

The information provided below was obtained from the manufacturer's website: http://erbitux.com/understand-erbitux.html.

For additional information, please request a copy of the current cetuximab package insert from your study doctor or visit: http://uspl.lilly.com/erbitux/erbitux.html.

Common:

- Rash, which can look just like acne, but which can be severe
- Fatigue
- Fever
- Skin changes, including dryness, itchiness, and cracking
- Inflammation of the skin around your finger and toe nails
- Mucositis / stomatitis (irritation or sores in the lining of the mouth and/or through the gastro-intestinal tract, which can become severe especially if cetuximab is given along with radiation)
- Infection
- Chills
- Difficulty swallowing
- Constipation
- Upset stomach
- Cough
- Electrolyte imbalance (low levels of magnesium in the blood)
- Increase in liver enzymes
- Increase in the amount of hair growth
- Sun sensitivity – you should avoid sun exposure while receiving cetuximab and for 2 months after the last dose

Infrequent:

- Allergic reaction, which can cause hives, shortness of breath, wheezing, or back pain
    - There is an increased chance of allergic reaction if you have a red meat allergy or history of tick bites.
- Nail changes

- Nausea and vomiting
- Dry mouth
- Diarrhea
- Weight loss
- Headache
- Tiredness
- Cardiopulmonary arrest – a temporary or permanent cessation of the heart
- Eye dryness or infection

Rare:

- Allergic reactions that can cause severe difficulty breathing, irregular heartbeat, low blood pressure, and can even be life threatening; in rare circumstances, this can lead to death.
- Sudden death
- Aseptic meningitis (inflammation of the layers that surround the brain)
- Interstitial Lung Disease which can cause inflammation in the lungs and breathing problems

Blood Draw:
Risks associated with the drawing of blood might include a small amount of pain from the puncture, bruising, bleeding, infection, or fainting. Every effort will be made to minimize discomfort.

IV insertion

Infrequent:

- Mild pain, discomfort, and/or bruising at the injection or needle insertion site
- Inflammation of the vein, as well as possible infection, bleeding, and soreness.

Rare:

- Severe pain, swelling, possibly an infection from the actual injection, fainting.

Biopsy:
The risks associated with a biopsy are soreness and discomfort. You may feel a stinging sensation each time the biopsy needle pierces the tumor. Serious bleeding and infection are very rare, but minor bleeding is relatively common. Alert your doctor immediately if the bleeding is heavy or prolonged. To prevent bleeding, your doctor may ask you to stop taking any medications that interfere with blood clotting, such as aspirin or Coumadin, before the biopsy. To prevent infection, you may be asked to take antibiotics before and after the procedure.

Reproductive risks:
You should not become pregnant or father a baby for the duration of your study participation and 60 days after the last dose of study drugs because the risks of receiving cetuximab and ficlatuzumab can affect an unborn baby. Women should not breastfeed a baby while on this study as harmful toxins can be passed to the baby through breastmilk. Women of childbearing age will have a pregnancy test within 14 days before beginning study treatment and again within 3 days of the first study treatment. Also, if applicable, breastfeeding must be discontinued if you are receiving the study drugs.

Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you are a female of childbearing potential and you choose to be sexually active, you should use an appropriate “double barrier” method of birth control (if your blood counts are not low and after

consulting with your doctor you may use a diaphragm, intrauterine device [IUD], or contraceptive sponge, in addition to male use of a condom with a spermicide), or you should be using prescribed “birth control” pills, injections, or implants, if found to be acceptable by your doctor.

If you are male and choose to participate in this study, your participation in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study. Medically acceptable contraceptives include surgical sterilization, or a condom used with a spermicide. You should inform your partner of the potential for harm to an embryo, fetus (unborn child). She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should promptly notify her doctor. Acceptable birth control methods must be used throughout the study and for 60 days after taking the last dose of study drugs.

If you plan to change your birth control method while you are on the study, you must notify your doctor before doing so. If you choose to be sexually active during this study, you need to know that even with use of these birth control measures pregnancy could still result.

The risks of receiving the study drugs while pregnant include potential loss of pregnancy or possible birth defects. If you become aware that you or your sexual partner is pregnant while you are taking part in this study, you must notify one of the doctors listed on this form immediately so that management of the pregnancy and the possibility of stopping the study drugs can be discussed

Allergies and/or Anaphylaxis Risks

While on the study you are at risk of experiencing an allergic reaction and/or anaphylaxis (severe reaction to a specific antigen) to the study treatments. Symptoms of an allergic reactions includes fever, chills, hives, rash, itching, joint pain, shortness of breath, low or high blood pressure, muscle stiffening, fainting, and sweating may occur during the injection/infusion and lasting about 24 hours.

Your doctor may give you additional medications to ease allergic and/or anaphylaxis reactions you may experience during the study. You should talk to your study doctor about these medications and any side effects you may experience while taking part in the study.

Radiation Exposure Risks:

CT scan: A CT scan is non-invasive, but involves exposure to radiation. There is a potential risk of radiation exposure from CT scans; this risk is considered small. Sometimes, an intravenous (in the vein) contrast dye is given with a CT scan. This contrast dye is iodine based. A person who has allergies is more likely to have an allergic reaction to the dye. This reaction may be mild, such as skin rash or hives to severe, such as breathing difficulties or shock. You will be closely monitored and treated should this occur. A severe allergic reaction would require immediate medical treatment and could result in permanent disability or death. You should discuss any history of allergies or concerns with your doctor. You may also experience discomfort related to lying still in an enclosed space for a prolonged period of time. The study staff prior to performing the procedure will provide additional instructions to you.

If you have questions or want additional information about risks and side effects, ask your study doctor.

What other choices do I have if I do not take part in this study?
If you do not wish to take part in this research study, your doctor will discuss alternate treatment options with you, including their benefits and risks. These may include:

- Treatment with other approved chemotherapy, or radiation therapies, if available and applicable to your disease
- Treatment with immunotherapy, specifically nivolumab or pembrolizumab, if you have not previously received it
- Taking part in another research study with drugs or radiation therapy, if available and applicable to your disease
- Getting treatment for your symptoms only, with no further cancer therapy. This is called comfort care, or palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel and tries to keep you as active and comfortable as possible.

Talk to your doctor about each of these choices before you decide if you will take part in this study. If you decide not to participate, withdraw your participation after starting the study, or if you are discontinued from this study, your doctor will discuss all other treatment options with you.

Can I stop being in this study?
Yes. You can decide to withdraw at any time. It is important to tell the study doctor if you are thinking about withdrawing so any risks from the ficlatuzumab or cetuximab can be evaluated. Another reason to tell your study doctor that you are thinking about withdrawing is to discuss what follow-up care and testing could be most helpful for you to help minimize side effects.

The study doctor may withdraw you from this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

When may participation in the study be stopped?
Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including:

- if it is in your best interest;
- you do not consent to continue in the study after being told of changes in the research that may affect you.

If you leave the study before the planned final visit, you may be asked by the study doctor to have some tests or procedures done so that you leave the study safely.

What happens if I am injured 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 Dr. Julie Bauman or the study coordinator at (520) 626-4101.

If you suffer an injury from taking part in this study, you should seek treatment. You or your insurance company will be billed for those services. If you do not have insurance, you will be financially responsible for those expenses. The University of Arizona has no funds set aside to pay for a research-related injury, added medical costs, loss of a job, or other costs to you or your family.

This, however, does not waive your rights in the event of negligence. If you suffer an injury from participating in this study, you should seek treatment. The University of Arizona and Banner Health have no funds set aside for the payment of treatment expenses for this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study

What are the costs of taking part in this study?
Some of the services you will receive and procedures you will undergo are being done only because you are participating in this research study. Examples of these "research-only" services and procedures include the study drug ficlatuzumab, research biopsy and the research blood work. The research-only procedures will be paid for by the study and will not be billed to you or your health insurance company.

Some of the services and procedures you will receive during the research study are considered "routine clinical services" that you would have received even if you were not participating in the research study. Examples are the physical exams, performance status evaluations, standard blood tests, the cetuximab, and radiological imaging to evaluate your disease. These "routine clinical services" will be billed to your health insurance company, but you will be responsible for paying any deductibles, co-payments, or co-insurance that are a normal part of your health insurance plan. If you do not have health insurance, you will be responsible for those costs. To obtain more detailed information about what routine clinical services your health insurance is likely to pay for, contact your insurance company.

Will I be paid for taking part in this study?
Your involvement in this research study is voluntary and you will not be paid for your participation.

Will my study-related information be shared, disclosed, and kept confidential?
The University of Arizona has rules to protect information about you. Federal and state laws also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

Information related to this research study that identifies you and your protected health information (PHI) will be collected from your past, present, and future hospital and/or other health care provider medical records. The Sponsor-Investigator will retain the specified records and reports for up to 2 years after the marketing application is approved for the investigational drug.

Any information about you obtained from this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked environment. You will not be identified by name in any publication of the research results unless you sign a separate consent form giving your permission (release).

The people working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may collect other information including your name, address, date of birth, phone number, social security number and other details. Photocopies of actual treatment records may be required as part of this review. By signing the consent form, you allow access to your medical records, without removal of identifying information such as your name, initials, date of birth, sex, race, and location of the research study.

Existing health records may include information related to the diagnosis or treatment of sexually transmitted disease (STD), acquired immunodeficiency syndrome (AIDS), human immunodeficiency virus (HIV), other communicable diseases, genetic information (e.g., genetic testing), and/or alcohol and/or drug abuse. The study staff and study sponsor's monitor may see this information while reviewing your regular health records for this study, but they WILL NOT create, collect, or disclose this type of information for the purposes of this research study.

Generally, only people on the research team will know that you are in the research study and will see your information. However, there are some exceptions, and the Principal Investigator may give information about you to people outside of the University of Arizona if required.

It is anticipated that there will be circumstances where your study related information and PHI will be released to persons and organizations described in this form. If you sign this form, you give permission to the research team to use and/or disclose your PHI for this study. Your information may be shared or disclosed with others to conduct the study, for regulatory purposes, and to help ensure that the study has been done correctly. These other groups include:

- Office for Human Research Protections or other federal, state, or international regulatory agencies
- Food and Drug Administration
- Banner University Medical Group and Banner Health
- The University of Arizona (UA) and the UA Institutional Review Board
- The sponsor supporting the study (the University of Arizona Cancer Center), their agents or study monitors
- In unusual cases, the investigators may be required to release your identifiable research information (which may include your identifiable medical record information) in response to an order from a court of law.
- Authorized representatives of the source of support of this study and manufacturer of ficlatuzumab, Aveo Oncology and their agents (Parexel and Biodesix), will review and/or obtain your identifiable information (which may include identifiable medical record information) for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data. While Aveo Oncology understands the importance of maintaining the confidentiality of your identifiable medical record information, we cannot guarantee the confidentiality of this information after it has been obtained by Aveo Oncology. The investigators involved in the conduct of this research study may receive funding from Aveo Oncology to perform the research procedures.
- Your primary care physician or a specialist taking care of your health.

Your PHI may no longer be protected under the HIPAA privacy rule once it is disclosed by the research team.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University of Arizona who receive your information may not be covered by this promise. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee this.

The Banner Medical Group (BMG) uses an electronic health record (EHR). Medical services (such as blood draws, CT scans, and MRIs) and test results completed by BMG for this research project will be placed in your EHR. If you do not have a BMG medical record, one will be created for you. It is necessary to create a medical record for services completed by BMG so that BMG can appropriately bill for the service. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your EHR as a result of your taking part in this study.

Study information (like questionnaires, diaries, and surveys) gathered directly from you by the researchers will be part of your research records but will not be added to your EHR. Your research records are kept separate from the EHR and available to research staff working on this study.

What study-related information and PHI will be obtained, used or disclosed from my medical record at Banner?
Information related to this research study that identifies you and your PHI will be collected from your past, present, and future hospital and/or other health care provider medical records.

The PHI you are authorizing to be used and/or disclosed in connection with this research study is:

- Your medical history
- Diagnostic information
- Lab and scan results
- Other information concerning treatment of your cancer

Demographic information to be disclosed may include, but is not limited to, your name, address, phone number, or social security number. If you receive compensation for participating in this research study, information identifying you may be used or disclosed as necessary to provide that compensation.

Your existing health records may include information related to the diagnosis or treatment of sexually transmitted disease (STD), acquired immunodeficiency syndrome (AIDS), human immunodeficiency virus (HIV), other communicable diseases, genetic information (e.g., genetic testing), and/or alcohol and/or drug abuse. The study staff and study sponsor's monitor may see this information while reviewing your regular health records for this study, but they WILL NOT create, collect, or disclose this type of information for the purposes of this research study.

When will my authorization expire?
There is no expiration date or event for your authorization. Therefore, unless you cancel this authorization (as instructed below) this authorization will continue to be effective.

Do I have to sign this authorization form?
You do not have to sign this authorization. However, if you decide not to sign, you will not be able to participate in this research study; and it will not affect any non-study Banner Health medical treatment or health care, payment, enrollment in any health plans, or benefits.

Also, by signing this form you are authorizing and permitting uses and/or disclosures of your PHI for future research purposes (e.g., future studies) as described in this document.

What do I need to know if I decide to cancel my authorization?

After signing the authorization, you may decide to cancel your previous authorization for the research team to use your PHI. If you cancel the authorization, you will no longer be able to stay in the research study. Please note that any PHI collected before you cancel the authorization may still be used. You may revoke the authorization by contacting the Principal Investigator in writing. Contact information is under "Who can answer my questions about the study" at the end of this document.

Will access be limited to your research study record during this study?
You may not have access to the research information developed as part of this study until it is completed.

Will my data or specimens be stored for future research?
About Using Tissue and Blood for Research
We would like to keep some of the tissue sample and blood for future research. If you agree, your tissue and blood will be kept and may be used in research to learn more about cancer and other diseases.

Your tissue and blood may be helpful for research whether you do or do not have cancer. The research that may be done with your tissue and blood is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

You tissue and blood samples will be de-identified; that is, they will be assigned a code and the information linking the code with your identity will be stored in a separate secure location. Your samples may be shared with secondary researchers without identifiers.

Reports about research done with your tissue and blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Your biological sample or genetic material may lead, in the future, to new inventions or products. If the research investigators are able to develop new products from the use of your biological sample or genetic material, there are currently no plans to share with you any money or other rewards that may result from the development of the new product.

Things to Think About
The choice to let us keep the left over tissue and your blood for future research is up to you. No matter what you decide to do, it will not affect your care or your participation in the main part of the study.

If you decide now that your tissue and blood can be kept for research, you can change your mind at any time. Just contact the investigator and let us know that you do not want us to use your tissue. Then any tissue or blood that remains will no longer be used for research and will be returned to the institution that submitted it or destroyed.

In the future, people who do research may need to know more about your health. While the institution/doctor may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are. Sometimes tissue and blood is used for genetic research (about diseases that are passed on in families). Even if your tissue and blood is used for this kind of research, the results will not be put in your health records.

Your genetic information is unique to you. You do share some genetic information with your family members. Although rare, there are examples where health insurers or employers have denied insurance or employment based on results from genetic testing. A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Your tissue and blood will be used only for research and will not be sold. The research done with your tissue and blood may help to develop new treatments for cancer and other diseases in the future.

Benefits
The benefits of research using tissue and blood include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks
The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

No matter what you decide to do, it will not affect your care.

Future Use of PHI and Samples (specimens)
Future research activity is part of this project. If you choose to participate in the future research activity your PHI will be included in this future research activity.

> By initialing the line below you agree to allow your information to be used and/or disclosed for the optional future research referenced above.
>
> _____ Initials

Who can answer my questions about this study?
If at any time you feel you have had a research-related injury, or for questions, concerns, or complaints about the study you may contact Dr. Julie Bauman or the study coordinator at (520) 626-4101.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Human Subjects Protection Program at 520-626-6721 or online at http://rgw.arizona.edu/compliance/human-subjects-protection-program.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Dr. Julie Bauman at (520) 626-4101.

If you have any questions or concerns about the authorization for access to your PHI, you should contact Sue Colvin, Banner Research Regulatory Affairs Director, at (602) 839-4583 or sue.colvin@bannerhealth.com. You may also request and will be provided a copy of the Notice of Privacy Practices.

To cancel your authorization for access to PHI you must notify the Principal Investigator in writing at the following address:

Julie E. Bauman, MD, MPH
University of Arizona Cancer Center
1515 N. Campbell Ave
Tucson, AZ 85724

An Institutional Review Board responsible for human subjects research at The University of Arizona reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

Research Biopsy Details
This section provides more detailed information about how the research biopsy is performed.

You have been asked to have a cup forceps biopsy or core needle biopsy (removal of a small sample of tissue from a mass or lump) as a part of this study.

Reason for the biopsy:
The purpose of this biopsy is to determine the type of tumor cells present and how your tumor cells react to the study treatment.

Biopsy Procedures:
All patients will be evaluated for the safety and feasibility of obtaining tumor tissue at the time of enrollment. If the performing physician agrees the biopsy can be safely performed using local anesthesia, you will have the procedure performed in the area of your primary tumor. The biopsy is done for the research, but standard procedures for this type of biopsy are followed. The biopsy will be performed by trained personnel. The biopsy may need to be done using ultrasound or CT guidance. The procedure will occur at the inpatient or outpatient office of the head and neck surgeon. The procedure may take 2-4 hours.

The procedure is done using local anesthesia (numbing of the skin). There are two methods for performing the biopsy: Cup biopsy or core biopsy. The cup biopsy involves a slender flexible forceps (scissor-like instrument) with movable cup-shaped jaws through a specially designed endoscope. The core biopsy involves the use of a 1 centimeter, 18-gauge hollow needle.

Both biopsy types involve:
- Preparation of the biopsy site with a skin cleanser such as isopropyl (rubbing) alcohol or iodine
- Injection of a local anesthetic (numbing medication), called lidocaine (a drug approved by the FDA), with the addition of a small amount of epinephrine (an FDA-approved drug) to constrict blood vessels, decrease bleeding, prolong anesthesia, and limit lidocaine toxicity

Core biopsy involves:
- Collection of three tissue specimens using the hollow needle.
- Dressing the site with Neosporin Cream (an FDA-approved drug) antibiotic ointment and a Band-Aid that should be removed in 24 hours.

Cup biopsy involves:
- This may be internal or external.
- A sharp tool is used to snip a part of your tumor.

The biopsy samples will be maintained by the investigators of this research project. To protect your confidentiality, all personal identifiers (i.e., name, social security number, birth date) will be removed (de-identified) and replaced with a specific code number. The information linking these code numbers to your identity will be kept in a separate, secure location. The investigators on this study will keep the samples indefinitely. Your biologic samples may be given to investigators outside of University of Arizona or may be utilized in future studies. If this is the case, they will remain de-identified.

If you have an allergy to lidocaine, (numbing medicine required for biopsy) we may use an alternative anesthetic. If the biopsy site is infected, it will be treated with antibiotic ointment and the biopsy will be postponed by 24 hours. If, at that time, the biopsy is still not possible due to infection, the biopsy will not be performed.

What are the possible risks, side effects, and discomforts of this biopsy?

Both procedures may leave a very small, fine scar, which usually fades with time.

Common:

- Pain from the procedure
- Bruising and soreness at the site of biopsy
- Scarring at the site

Rare:

- Infection and bleeding

Signing the consent form

I have read (or someone has read to me) this form, and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study and I authorize the use and/or disclosure of my PHI. I am not giving up any legal rights by signing this form. I will be given a signed copy of this form.

Printed name of subject	Signature of subject	Date

Investigator/Research Staff

I have explained the research to the participant or the participant's representative before requesting the signature(s) above. There are no blanks in this document. A signed copy of this form has been given to the participant or to the participant's representative.

Printed name of person obtaining consent	Signature of person obtaining consent	Date

HSPP Use Only:
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