Official Title	Intraoperative visualization of oral cavity squamous cell carcinoma and high-grade dysplasia with tozuleristide, a fluorescent tumor marking agent
NCT Number	NCT05316688
Document Type	Informed Consent Form
Document Date	3/11/2025

University of Washington Medical Center

Consent to take part in a research study:

An Intraoperative visualization of oral cavity squamous cell carcinoma and high-grade dysplasia with tozuleristide, a fluorescent tumor marking agent

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Emergency number (24 hours): 206-598-6190

Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to obtain more information about the safety and efficacy of an imaging drug, tozuleristide, which is used with a standard of care fluorescent imaging device, when used during surgery to remove oral cavity cancer.

People who agree to join the study will be asked to attend a clinic visit before surgery, a visit in the preoperative area where tozuleristide will be administered, and a clinic visit after surgery. The study will span approximately 7 weeks. The study involves looking at your tumor under fluorescent imaging in the operating room to see if this technology can help surgeons distinguish normal tissue from tumor. You will receive an injection before surgery of the fluorescent contrast drug, and the safety of the drug will be monitored throughout the study. We will also investigate the images and pathology we get from the tissue samples removed during surgery.

We do not know if tozuleristide would help treat oral cavity cancer, and side effects could even make your condition worse. Tozuleristide could cause side effects such as nausea, headache, diarrhea, or changes in laboratory values as described below in this form.

You do not have to join this study. You can choose to receive standard methods to treat oral cavity cancer instead of participating in this study. We will give you details about the purposes, procedures, risks, and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research study because you have oral cavity cancer.

Approximately 15 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say “yes” or “no”, or to drop out after joining. If you say “no,” you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

We are doing this study to find out more information about the imaging drug, tozuleristide, when it is administered to people with oral cavity cancer and used with a fluorescent imaging device during surgery of oral cavity cancer. We want to know how well tozuleristide works at detecting tumors during surgery. This study will also look at the safety of using tozuleristide for surgery. We want to find out whether there are any side effects or changes to laboratory results or vital signs associated with the drug. We will also investigate whether fluorescence from tozuleristide can help surgeons distinguish normal tissue from tumor tissue by examining the images and pathology from the tissue samples removed during surgery.

Tozuleristide is an experimental drug that is thought to attach to tumor cells. It is given by injection into a vein. It contains a dye that fluoresces, or glows, under a specific kind of light from an imaging camera. The process of shining light on tozuleristide to make it glow is called “fluorescence imaging”. It is sometimes difficult for surgeons to distinguish normal tissue from tumor tissue during surgery or to see if the tumor has spread to other areas. The goal of tozuleristide is to help surgeons to better see the difference between normal and tumor tissue during surgery using fluorescence imaging.

Tozuleristide has been tested in adults with skin, breast, and brain tumors and in children and young adults with brain and spinal cord tumors. Tozuleristide has not yet been studied in humans with oral cavity tumors.

In this study, we want to learn:

- If tozuleristide can be safely used for oral cavity cancer. If you join this study, we would give you tozuleristide, then image your tumor with a suitable standard of care fluorescent imaging system during surgery. We will watch carefully for any side effects.

- All participants in this study will receive the same dose of tozuleristide. This dose has been used in adults with other types of cancer in previous studies. We will watch carefully for any side effects.

- We also want to study the efficacy that tozuleristide has on surgery for patients with oral cavity cancer.

What research tests, procedures, and treatments are done in this study?

If you join this study, we will do the following tests and procedures:

Within 30 days prior to your surgery	**Before surgery (1-30 hours)**	**Day of surgery (Day 1)**	**7 to 21 days after surgery**
• Screening, including*: -Medical history -Physical examination -Laboratory tests	• Pregnancy test* • Administration of study drug	• Surgical resection of tumor* • Imaging with a suitable fluorescent imaging device	• Physical examination*

*History, physical examination, and surgery with surgical pathology are a routine part of your care. Pregnancy test for females of childbearing potential is also routinely performed prior to surgery.

Within 30 days before your scheduled surgery:

The screening exams will include the following:

- Demographic data (e.g., age, race and sex)
- Physical examination
- Complete medical history, including baseline conditions
- Performance status - assessment of your ability to perform everyday tasks

Pre-Surgery (between 1 and 30 hours before your scheduled surgery)

- Blood or urine pregnancy test if you are a female of childbearing age
- Study drug administration – An intravenous (IV) cannula (thin plastic tube) will be inserted in the vein, usually in the hand or arm, to allow administration of pre-operative drugs. Having an IV is a routine part of your care before surgery. Tozuleristide will be administered through your IV. You will receive a dose of 12 mg. The dose of tozuleristide will be administered in a one-time IV injection no less than 1 hour and a maximum of 30 hours before you undergo surgery. The injection will take about 1-5 minutes.

Day 1 (day of surgery)

- Your surgery will be performed according to standard of care. This means your surgeon will follow their normal practices and use their best clinical judgement for how to access and remove (resect) your tumor. During your surgery, the surgeon will make note of which tissue they think is tumor and how much tissue they believe should be removed in order to get all of the tumor out. A picture will be taken with the fluorescent imaging system under regular light conditions and with the special light from the imaging device that makes tozuleristide fluoresce, or glow. The surgeon and research staff will note whether the tissue that they believe is tumor is glowing or not. There may also be tissue that your surgeon is not sure whether or not is tumor. These areas may be sampled as part of your routine surgery, and they will be labeled so that the research team can keep track of fluorescence information of any tissue that was removed.
- After your tumor is removed, additional pictures will be taken using normal light and fluorescence light with the imaging device. Any fluorescence will be noted by the surgeon and research team.
- During your surgery, it is possible that any images taken and tissue fluorescence will draw your surgeon's attention to certain areas of your oral cavity. It is possible that the fluorescent areas may contain normal tissue, removal of which may lead to adverse functional or cosmetic outcomes. The surgeon may investigate these areas, but it is always the surgeon's decision, using their best judgement with normal light conditions, about whether it may contain tumor and what to remove and what to leave. All tissue removed will be for the purpose of your routine surgical care. Your surgeon will not change surgery or take tissue just for research.
- During surgery, your tumor and nearby areas may also be video recorded using a video recorder that is part of the imaging system. This is to collect data for study purposes. The video recording may also be used for publications and to train future investigators on the use of fluorescent imaging and tozuleristide. For the surgery, your body and face will be covered with sterile drapes, so only the area to be treated is visible to the surgeon (the surgical field). When the video recording starts, only the surgical field will be exposed. This means that the video recording will not record your face or anything else that can be used to identify you. Representatives from Blaze Bioscience may be present in the OR during your surgery to assist with fluorescent imaging.
- After your surgery you will be taken care of by your surgeon and hospital staff according to regular standards of care. In the days following your surgery, your doctor will discuss the results of your tumor diagnosis and surgery with you. However, you will not receive all of the results from the research tests conducted on your tumor.

7-21 days after surgery

You will be seen in clinic for a routine post-operative visit 7-21 days after surgery. In addition to collecting information about any interval changes with your medical history, a physical examination will be performed.

If you join this study, you would stay in this study for a maximum of 3 weeks after your surgery. After surgery, you will have a follow-up visit in clinic 7-21 days after surgery.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. Tozuleristide could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

If you join this study, we would tell you if we discover new side effects that could affect you.

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop taking tozuleristide. In some cases, side effects can last a long time or never go away.

Known Potential Risks (in order of likelihood):

Immediate risks (reported in 1-2 patients who have received tozuleristide):

- Nausea
- Headache
- Hypertension/high blood pressure
- Diarrhea and/or frequent bowel movements
- Abdominal (stomach) pain or discomfort/bloating
- Vomiting
- Changes in laboratory values including changes in liver tests (ALT/AST), alkaline phosphatase, albumin, or protein in the urine
- Altered taste sensation
- Green discoloration of urine

- Itching and/or rash of the skin
- Injection site pain
- Acneiform

Other possible immediate risks:

- Photo-irritation/photo-toxicity: Studies in humans have not shown any side effects related to photo-irritation or photo-toxicity. However, this is still a theoretical risk given that tozuleristide contains a fluorescent dye designed to absorb light. Thus, it is recommended that after receiving the drug you protect yourself from sun exposure through the use of appropriate clothing, sunscreen, sunglasses, etc.
- Highlighting normal tissue as potentially abnormal
- Not highlighting tumor tissue

Long-term risk:

- Discoloration of tissue including kidney and lymphatic tissue

You should know that no studies have been done to assess the potential of the dye component of tozuleristide to cause mutations or cancer. However, indocyanine green, which is the fluorescent part of tozuleristide, is approved by the United States Food and Drug Administration (FDA) and has been safely used in humans for over 50 years.

Unknown Risks of tozuleristide:

There also could be other side effects or risks that we do not know about yet. Many side effects may go away shortly after the study medication is stopped. But in some cases they can be serious, long-lasting, permanent, and/or fatal. A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research during the study. As information becomes available subjects will be told of any changes in the way the study will be done and of any newly identified risks that might affect their participation in this study.

If you participated in this study previously and received tozuleristide are now planning to receive another dose of tozuleristide, you could experience side effects even if you did not experience them the last time you received tozuleristide. There may be an added risk of an allergic reaction even though you did not experience one the first time you received tozuleristide. Symptoms of an allergic reaction can include headache, rash, hives, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe but rare allergic reactions can cause dizziness, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. The medical staff will watch you carefully during and after your injection. If you have symptoms of an allergic reaction after you leave the hospital, you should contact the study doctor or study staff immediately. Another potential

risk of a second dose is that your body's immune system may form a protein that could make tozuleristide ineffective. In this case your tumor may not uptake the second dose of tozuleristide.

Reproductive risks:
Taking part in this research study can affect an unborn baby because the research study drug could harm an unborn baby. Because of this, you should not become pregnant or father a baby while on this study or for 30 days after this study ends. Both male and female participants of child bearing potential who engage in sexual activity must use 2 reliable methods of contraception simultaneously until 30 days after receiving study drug. Tozuleristide might involve risks to an embryo or fetus, which are currently unknown. It is important that you contact the study doctor or the study staff immediately if you believe you might be pregnant. Females of childbearing potential in the study will have pregnancy tests before receiving tozuleristide. You and the study doctor should discuss and agree on how you will prevent pregnancy.

If you join the study and have a positive pregnancy test, we would tell you about the test results. If you have a positive pregnancy test, we would ask you to leave the study.

If you are a male participant and your female partner becomes pregnant during the study, we will ask your female partner for consent and authorization to collect information on the outcome of her pregnancy and the status of your child, including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, abnormalities, or complications. This information will be collected from your female partner's medical records with her permission.

Blaze Bioscience has not tested whether tozuleristide is present in breast milk or the effects of tozuleristide in breast-fed infants. You should not breastfeed a baby while on this study and for 30 days after surgery.

Risks Related to Fluorescent Imaging Systems

The following are potential risks that could occur when using fluorescent imaging systems.

- Highlighting normal tissue as potentially abnormal
- Not highlighting tumor tissue
- Failure to display white light and/or fluorescence images
- Interfering with the normal operation of the surgical microscope
- Interfering with surgical procedure
- Extending surgical procedure time
- Physical injury due to imaging head falling due to failure to mount properly on the surgical microscope
- Risk of laser light leakage from the laser source, cable and/or head

- Electrical shock hazard to the user
- Increased tissue heating
- Risk of infection from non-sterile imaging head

Risks Related to Study Procedure

The following is a list of medical procedures that will be performed and their associated risks.

Injection Risks

Injection is a way of putting fluids into the body using a syringe and a hollow needle that is poked through the skin. Reactions could include bruising, pain, bleeding, and rarely infection at the injection site, feeling lightheaded and fainting. As with any injection there may be some irritation at the injection site where the study drug is administered.

Incidental Findings

It is possible that the research procedures could uncover information related to your health that you did not know about before and that is unrelated to the Study. Some of these findings may be too preliminary to share. The University of Washington will carefully consider the research findings and determine if they should be shared with you. In some cases, additional clinical testing may be required. The cost of any additional testing and any related treatment will be your responsibility.

What are the benefits?

Taking part in this research study may or may not make your health better. If your tumor tissue is easier to see after you receive tozuleristide, it is possible that tozuleristide will improve your surgeon's ability to remove all tumor tissue while leaving healthy tissue intact. We hope the information learned from this research study will help others with oral cavity tumors in the future by helping us to learn more about the safety and efficacy of tozuleristide for identifying and resecting oral cavity tumors.

You have other choices besides this study.

Taking part in this study is voluntary. You may choose to not be in this study. If you decide not to be in this study, or discontinue your participation, there is no penalty, and you will not lose any benefits to which you are entitled. You will still receive medical care. If you decide to stop participating in the study, your data collected up through that time will remain part of the study database and may not be removed. In addition, we will ask you if you want to provide further data collection from routine medical care.

If you decide not to take part in this study, you have other choices. The researcher will discuss these options and their risks and benefits with you.

For example:

- you may choose to be treated with the usual clinical approach (surgical removal of your tumor without participating on the study)
- you may decide to not be treated

Enrollment in this study may exclude you from other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis.

They include:

- Researchers involved with this study.
- Blaze Bioscience (funder of the study and provider of tozuleristide) and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- The University of Washington.
- Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, we are required to report certain sexually transmitted diseases and HIV infection. We also have to report suspected abuse or neglect of children and vulnerable adults. Workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study.

You will not be charged for the costs of the special studies (research tests) that are being done for research purposes only, such as submission of your data or tissue to the study team. Tozuleristide will be provided by the study at no cost to you or your insurance company.

What if you get sick or hurt after you join this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact 206-598-6190. They will treat you or refer you for treatment.

The researchers have taken steps to monitor and minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed about any injuries, side effects, or other problems that you have during this study as soon as possible. You should inform the researchers of any new medication (prescribed or over the counter) that you are taking. You should also tell your regular doctors that you are participating in a research study.

If you become sick or injured as a direct result of the proper administration of tozuleristide, Blaze Bioscience will reimburse for the reasonable and necessary study-related costs of such medical treatment, provided that:

- The sickness or injury is not caused by your failure to follow the instructions of the study staff.
- The costs are not the result of care required to treat your underlying disease or condition.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You will not lose any legal rights by signing this form.

What will my information and/or tissue samples be used for?

Your information and tissue samples (such as blood and tumor cells) will be used for the purposes of this study. Any side effects related to this study will also be recorded. Tissue taken from surgery will be used to correlate fluorescence with presence or absence of tumor on pathology. The pathology report from these samples will appear in your electronic medical record. Data collected from the tissue samples for the purposes of the study will be deidentified.

Any tissue samples removed during surgery are removed permanently and you relinquish all data and proprietary rights therein upon sample removal.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, we do not expect any test results that would affect your care, so we do not plan to return results to you.

Will my information and/or tissue samples ever be use for future research?

Your information and tissue samples (even if made anonymous) will not be used for any research other than this study.

Your rights

- You do not have to join this study. You are free to say “yes” or “no”.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- If you decide to drop out, we would want you to tell the study doctor.

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

Your responsibilities

If you join this study, you will have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy.
- Tell us about side effects.

For more information

If you have questions or concerns about this study, you can talk to your doctor anytime. Other people you could talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-520-5000 Dr. Emily Marchiano, PI 206-598-6190 Emergency number (24 hours)
If you get sick or hurt in this study	206-598-6190 Emergency number (24 hours) Rebecca Wood Research Mgr. (206) 606-6970
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	The financial services department at (206) 520-0400

Emergency number (24 hours): 206-598-6190

Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant:

Printed Name	Signature	Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name	Signature	Date

If you served as an interpreter or witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

Witness Interpreter Printed Name	Signature	Date

Protocol: BB-IST002
Current consent version date: 14FEB2025
Previous consent version date: 06JUN2023
Copies to: Participant and Medical Record