Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH: Exploratory clinical trial of topical Imiquimod 5% cream as window-of-opportunity monotherapy for early-stage oral cancer

MUSC CTO # 103625
Principal Investigator: Angela Yoon, DDS

You are being asked to participate in a research study. This document will explain what the study is about, what you will be asked to do, and the risks and benefits of participating in the study so that you can make a decision whether or not you want to participate. Your participation is voluntary, which means you can decide whether or not you want to participate. If you decide not to participate, your care at Medical University of South Carolina will not be affected and your doctor will discuss your treatment options. You will be given a copy of this form to take home and discuss with your family, friends, or your doctor. If you have any questions, you should ask the study team. If you decide to participate, you will be asked to sign a copy of this form.

- We are asking for your consent to voluntarily participate in this study.
- The purpose of this research study is to find out what effects, good and/or bad, topical application of the study drug Imiquimod will have on you and your oral cancer.
- You will need to come to see your study doctor to see if you are eligible for the study, and if you are, you will have a Day 1 tele-visit (by phone), and Day 14 and Day 29 clinic visits. At the clinic visits, report any side-effects you have experienced to your study doctor. You will have oral exams and pictures taken of the growths, inside your mouth. You will be in this study for about 8 weeks.
- You will receive Imiquimod for a maximum of 28 days until your scheduled surgery. If you stop using Imiquimod cream due to unacceptable side effects or cancer growth, your study doctor will continue to watch you for side effects and follow your condition for at least 30 days or until the side effect has resolved. Your surgery will proceed as initially scheduled but the doctor will follow your progress.
- The most likely side effect of the study drug is the irritation of the treatment site, such as redness, itching or burning.
- You may not directly benefit from the study drug, but there is a possibility that the treatment you receive may prove to be effective in shrinking the size of tumor before the surgery, although this cannot be guaranteed.
- The alternative is to receive clinical care, which may include surgery, without participating in this study.

In summary, you will receive Imiquimod for 28 days until your scheduled surgery if you are tolerating the study drug and your cancer is not growing while receiving the study drug. If you stop using Imiquimod cream due to unacceptable side effects or cancer growth, your study doctor will continue to watch you for side effects and follow your condition for at least 30 days or until the side effect has resolved.

A. PURPOSE OF THE RESEARCH

The purpose of this research study is to find out what effects, good and/or bad, topical application of the study drug Imiquimod will have on you and your oral cancer. Imiquimod is a drug that activates toll-like receptor (TLR) in oral cancer cells causing self-destruction of tumor cells. It also activates immune cells to attack and eliminate cancer cells. Imiquimod is currently approved by the Food and Drug Administration (FDA) for treatment of skin precancer and cancer, as well as genital and perianal (around the anus) warts. There is only limited information on whether imiquimod can be used in mouth cancers. Its use in this study is not approved by the FDA and is considered investigational for the purposes of this study.

In this exploratory study, we want to find out if we can give Imiquimod topical cream for four weeks before your scheduled surgery. Specifically, we want to find out if there is considerable shrinkage of oral cancer with 28 days of Imiquimod application. A grant from the National Institutes of Health (NIH) will sponsor this study. Portions of Dr. Yoon and his research team's salaries will be paid by this grant.

Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. You are being asked to participate in this study because you are/have oral cancer. The investigator in charge of this study at MUSC is Dr. Yoon. The study is being done at MUSC only. Approximately 15 people will take part in this study.

B. PROCEDURES

You will have your first consultation with the head and neck surgeon to go over your current condition and treatment options. He/she will conduct physical examination and may order scan of your body (PET scan; an imaging test that allows your doctor to check for disease in your body) as standard of care. He/she will also schedule the surgery date in 4 weeks after the first day of Imiquimod treatment.

Most of the exams, tests, and procedures you will have are part of the usual approach for your condition. However, there are three extra oral exams that you will need to have if you take part in this study.

If you agree to be in this study, the following will happen:

1. We will request the following during the screening visit to find out if you can be in the study.

   - Previous biopsy result showing evidence of oral cancer
   - Oral examination to measure size of tumor and take picture
   - A complete list of your current medications including vitamins and supplements to your study doctor as some medications may interact with Imiquimod and your study doctor will need to be aware of what drugs, vitamins and supplements you are currently taking
   - Blood pregnancy test in women of child-bearing potential. Approximately one teaspoon of blood will be collected for a blood pregnancy test.
     - If you are a woman of childbearing potential and /or a man capable of fathering a child before, during, and/or after, participation precaution should be taken. Examples of acceptable methods of birth control for participants involved in the study includes birth control pills, patch, IUD, condom, sponge, diaphragm with spermicide, or avoiding sexual activity that could cause you to become pregnant.

3. If the oral and physical examination show that you are eligible for the study, you will be asked to take blood test (a measure of your health by a full blood count) in which approximately one teaspoon of blood will be drawn. You will also be given instruction as to how to apply the medicine and a daily diary form.

4. You may pick up your study medication in person, or it can be mailed to you, if that is preferred and the study doctor will call asking you to start applying the medicine. You will be asked to keep a daily diary to track the use of study drug once a day. The drug can be applied using your finger or Q-tip. Remember to wash your hands after drug application.

   Please abstain from eating or drinking for at least 30 minutes after application of topical imiquimod cream

5. Fourteen (14) days after the first use of the study drug, you will be asked to come in for an oral exam. At this time, we will measure the tumor size to see if there is any change and take a picture. We will also ask if you had any side effects using the medicine. This procedure will take about 30 minutes.

6. Twenty-nine (29) days after the first use of the study drug, you will be asked to return for a final oral exam. Again, we will measure the tumor size to see if there is any change and take a picture. We will also ask if you had any side effects using the medicine. You will be asked to provide the list of any other new medicine used since the study start time. The daily diary form you completed, and any unused study drugs should be returned to your study doctor on this visit. This procedure will take about 40 minutes.

7. We will collect results or your pre-surgery blood tests from your medical record to use as a comparison to your blood work obtained at the beginning of the study.

8. Sixty (60) days after enrollment, we will contact you to see how you are doing.
9. Your medical record will continue to be reviewed until you complete the study (approximately 8 weeks after consent).

C. DURATION

Participation in the study will take about 3 visits over the period of 4 weeks. You will remain in the study, to include the follow up period, for a total of 8 weeks.

D. RISKS AND DISCOMFORTS

Common adverse events (side effects) are:

- Redness, itching, burning, or bleeding of the treated area (33%)
- Flaking, scaling, dryness, or thickening of the skin (33%)
- Swelling, stinging, or pain in the treated area (33%)
- Blisters, scabs, or bumps on the skin (33%)

Less common adverse events (side effects) are:

- Headache (11%)
- Inflammation or swelling of the tissue lining the sinuses (7%)
- Diarrhea (3%)
- Red and itchy skin reaction (2%)
- Back pain (1%)
- Tiredness (1%)
- Irregular and rapid heat rate (1%)
- Virus infection (1%)
- Dizziness (1%)
- Vomiting (1%)
- Infection of any part of urinary system (1%)
- Fever (1%)
- Tremor caused by a chill (1%)

Some side effects can be serious. If you experience any of these symptoms, call your study doctor immediately:

- Flu-like symptoms such as nausea, fever, chills, tiredness, and muscle weakness or pain (15%)

LOSS OF CONFIDENTIALITY

There is a risk of loss of confidentiality since medical records will be reviewed during this study. MUSC and its study team members will take every effort to ensure that your information is kept confidential during this study.

PREGNANCY RISKS

It is not know what effects, if any, Imiquimod cream would have on pregnancy or a fetus. Therefore, women should avoid becoming pregnant during the course of the study.

E. MEDICAL RECORDS AND CERTIFICATE OF CONFIDENTIALITY

If you are an MUSC patient you have an MUSC medical record: If you have never been an MUSC patient, a MUSC medical record will be created for the purposes of this study. Results of research tests or procedures will be included in your MUSC medical record. All information within your medical record can be viewed by individuals authorized to access the record We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law.

This research is covered by a Certificate of Confidentiality from the Federal government. This means that the researchers may not disclose information or biospecimens that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, nor can the information or biospecimens be used as evidence, unless you have consented to this disclosure. Information or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you are an MUSC patient you have an MUSC medical record. If you have never been an MUSC patient, a MUSC medical record will be created for the purposes of this study. Results of research tests or procedures will be included in your MUSC medical record. All information within your medical record can be viewed by individuals authorized to access the record. We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law; however, there is the possibility that your research information will be disclosed.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, or harm to self or others

Finally, a Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating Federally funded projects or information needed by the FDA.

F. BENEFITS

The potential benefit to you is that the treatment you receive may prove to be effective in shrinking the size of tumor before the surgery, although this cannot be guaranteed.

G. COSTS

There will be no additional costs to you because of being in this study. However, routine medical care for your condition (care you would have received even if you were not in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further. It is possible that your insurance company will refuse to pay for the costs associated with study participation, in which case you will be held financially responsible. Please ask Dr. Yoon if you would like to know more about which tests and studies are being done solely for research purposes.

H. PAYMENT TO PARTICIPANTS

You will not be paid for participating in this study.

I. ALTERNATIVES

The alternative is to receive clinical care, which may include surgery, without participating in this study.

J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

K. DISCLOSURE OF RESULTS

Clinically important results, such as tumor becoming larger or smaller, will be disclosed to you.

L. AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, your study doctor and her research team will keep records of your participation in this study.

The health information MUSC may use or disclose (release) for this research study includes information in your medical record, results of physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study.
- Other institutions and investigators participating in the study.
- Data Safety Monitoring Boards.
- Accrediting agencies.
- Clinical staff not involved in the study whom may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment.
- Federal and state agencies and MUSC committees having authority over the study such as:
    - The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.
    - The United States Food and Drug Administration ('FDA') and/or the Office of Human Research Protections ('OHRP')
    - National Institute of Health (NIH), an institution that will be able to inspect and collect your clinical data and/or samples.

In addition to this study, you have the option of participating in future storage of your tumor tissue specimens, for possible genetic study. Your protected health information may be used or shared with others outside of MUSC for this research as well. Please initial below if we may use/disclose your protected health information for the optional research portion/s of this study.

_____Yes, you may use my protected health information for the optional research portions of this study.

_____No, you may not use my protected health information for the optional research portions of this study.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study or, if you are participating in a study designed for the development of a drug or device, your authorization will remain in effect until the drug or device is approved by the FDA or until the company's application to study the drug/device is withdrawn. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

Your health information will be used or disclosed when required by law. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and for conducting public health surveillance, investigations or interventions. No publication or public presentation about the research study will reveal your identity without another signed authorization from you.

If you have questions or concerns about this Authorization or your privacy rights, please contact MUSC's Privacy Officer at (843) 792-8740.

M. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

N. CLINICAL TRIALS.GOV

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.

O. COLLECTION OF SPECIMENS

As part of this study, we would like to store tumor tissue specimens collected from you for future research on oral cancer. This future research may be conducted by Dr. Yoon or by other researchers who obtain IRB approval for their research. This research may involve genetic studies. Part of the tissue collected will go to Dr. Yoon for a related study that will evaluate the effect the study drug has on immune cells.

There are several things you should know before allowing your tissues to be studied or to be stored.

1. The tumor tissue specimens will be labeled with a code that only study personnel can link back to you. Researchers outside of this study will not be given a link between the code number and your name or any other identifying information. While we hope this will prevent any potential loss of privacy or confidentiality, we cannot make any guarantees.
2. In addition to your name, other information about you might be connected to your sample. For instance, information about race, ethnicity, sex, your medical history, and so forth might be available to investigators studying your specimen. Such information might be important for research or public health. It is possible that this information (including genetic information) might come to be associated with your racial or ethnic group.
3. The specimens obtained from you in this research may help in the development of a future commercial product. There are no plans to provide financial compensation to you should this occur.
4. Investigators in this study may try to re-contact you in the future to find out about your health. If you are contacted and want to know what the investigators have learned about your samples, you should understand that the following are the kinds of things the investigators or your health team might tell you:
    a. Information is too preliminary to give you details, but you will receive a newsletter informing you about the results of the project.
    b. For any future research, we may contact you with a new consent form giving you additional information.
    c. You carry a gene for a particular disease that can be treated.
    d. You carry a gene for a particular disease for which there is no current treatment. This news might cause severe anxiety or other psychological distress, depending on the severity of the disease.
    e. You carry a gene for a disease and might consider informing relatives that they, too, might carry the gene. It can be very difficult to decide whether to share such information with relatives. Genetic counselors can help sort out the various options in such a case.

You may request at any time that your research samples be removed from storage and not be used for future research. If you decide you want your samples removed, you may contact Dr. Yoon via written communication at the following address: 39 Sabin St., Walton Research Bldg. 7th Floor, Charleston SC 29425. Once the request is received, and if your samples have not already been used for other research, they will be destroyed. If you do not make such a request, your specimens will be stored indefinitely or until completely used.

Initial your choice below:

_____Yes, I agree to allow my samples to be kept and used for future unknown research, and I also allow Dr. Yoon to use part of the sample to study immune cells.

_____No, I do NOT agree to allow my samples to be kept and used for future unknown research, and I also do NOT agree to allow Dr. Yoon to use part of the sample to study immune cells.

P. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below:

_____Yes, I agree to be contacted

_____No, I do NOT agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The sponsor and the Food and Drug Administration (FDA) will receive copies of the research records. The investigators associated with this study, employees of the sponsor, the FDA, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event of a study related injury, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and

tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. The data collected on you to this point remains part of the study database and may not be removed. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Yoon at 843-792-4271. I may contact the Medical University of SC Patient and Family Care Liaison (843) 792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

_____ _____

Signature of Person Obtaining Consent Date *Name of Participant

_____

Signature of Participant Date