TITLE: Phase 1/2, Open-Label, Single-Arm, Safety and Efficacy Dose-Finding, Systemic Exposure, and Device Technical Effects of PRV111 (Cisplatin Transmucosal System) in Subjects with Oral Squamous Cell Carcinoma

NCT NUMBER: NCT03502148

DATE: 28FEB2020

[redacted]

Consent to Participate in Human Research

Informed Consent Form

TITLE: Phase 1/2, Open-Label, Single-Arm, Safety and Efficacy Dose-Finding, Systemic Exposure, and Device Technical Effects of PRV111 (Cisplatin Transmucosal System) in Subjects with Oral Squamous Cell Carcinoma

PROTOCOL NO.: CLN-001
[redacted]

SPONSOR: Privo Technologies, Inc.

INVESTIGATOR: [redacted]

STUDY-RELATED PHONE NUMBER(S): [redacted]

SUBJECT NAME: _____ **Date of Birth:** _____

Introduction

You are being asked to take part in a clinical trial, a type of research study, of an investigational product (PRV111) because you have been diagnosed with oral cancer. Clinical trials include only people who choose to take part. Please take your time to understand the study, ask questions and then make your decision. You may discuss your decision with your family, friends and your health care provider. If you have any questions, you can ask your study doctor for more explanation.

Before you learn about the study, it is important that you know the following:

- Your participation is entirely voluntary.
- You may decide not to participate or, if you do participate, you may withdraw from the study at any time. You may decide not to participate or to withdraw your consent without anyone objecting and without penalty or loss of any benefits that you are otherwise entitled.
- There may be unforeseeable risks and side effects of PRV111 that are not yet known. If any new information is learned or the study is changed in a way that could affect your

willingness to participate, you will be told about the change(s). You may be asked to sign a revised informed consent form.

- 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.

Once you understand the study and its possible risks and benefits, if you decide to participate, you will be asked to sign and date this informed consent form. You will receive a copy of the informed consent form. By signing it you are telling us that you:

- Understand what you have read;
- Consent to take part in the study;
- Consent to the tests and treatments that are described;
- Consent to the use of your personal and health information and biological samples, as described.

Why is this study being done?
The purpose of this study is to evaluate the safety, tolerability and anti-tumor effects of the PRV111 chemotherapy patch. The PRV111 patch includes a chemotherapy drug called cisplatin, which is a Food and Drug Administration (FDA) approved drug that is known to be effective for oral cancer. Cisplatin is usually injected into the bloodstream intravenously (an injection in to your vein) to treat oral cancer. PRV111 includes cisplatin within a patch applied in your mouth and is designed to keep the drug locally to the tumor tissue.

Study Description
You are being asked to be a part of this study because you have been diagnosed with oral cancer.

Up to 31 subjects will be enrolled in the United States. All subjects will receive PRV111.

Your participation in the study will be for approximately 9 months. This will consist of up to 28 days to perform assessments to assess your eligibility called Screening. If you qualify and choose to be part of the study, you will receive the treatment [redacted] prior to your scheduled surgery. After the surgery, you will be asked to return at 1 month, 3 months and 6 months for the study doctor to monitor your progress and check for any possible issues. **(NOTE: There will be other standard consent forms for your surgery.)**

Prior to surgery, you will have 4 treatment visits and will receive either 3 or 5 treatment applications of the PRV111 patch. [redacted] These applications will take approximately 35 minutes. The 4 treatment visits will be separated by 2 to 6 days (at least 48 hours between visits).

What will happen if I take part in the study?
After you sign this consent form, you will begin the first part of the study called Screening. You will have the following assessments:

- Answer questions about your medical history including past and present illnesses, drug and alcohol use, all prescribed medications, over-the-counter medications and supplements you have taken in the last 30 days
- A physical examination that includes examination of your mouth and neck
- Confirmation of cancer diagnosis as standard of care.
- Checking for presence of human papillomavirus (viral infection passed from skin-to-skin contact) from tumor tissue collected as standard of care.
- Vital signs (heart rate, blood pressure and oral temperature) and height and weight
- A 12-lead electrocardiogram which is a test used to measure the electrical activity of the heart, after resting for at least 10 minutes
- Computed tomography (CT) scan or magnetic resonance imaging (MRI) of your head and neck, and a CT scan of your chest
- Provide blood and urine samples for routine safety labs
- If you are a woman and able to get pregnant, you will provide a sample (blood) for a pregnancy test. The results of the pregnancy test must be negative in order for you to be in the study

After all the study assessments are performed and if your study doctor considers this study suitable for you, you will be invited to return to the clinic on Treatment Visit 1.

Treatment Visits 1, 2, 3 and 4
You will return to the clinic and the following assessments will be performed:

<u>Prior to receiving drug:</u>

- A physical exam that includes examination of your mouth and neck
- Tumor measurement and photographs
- Provide blood and urine samples for routine safety labs (Visits 1 and 3 only)
- Provide a blood sample to find out what happens to the study drug in the body called pharmacokinetics
- Urine pregnancy test for women (Visits 1 and 4)
- The study doctor may numb your tongue prior to applying the study drug to prevent your tongue from removing the patches

Once these assessments are performed, a clinic staff member will begin applying the PRV111 patches in your mouth.

After receiving drug:

- Ask you how you are feeling [redacted]
- Report any medication you have taken
- Provide a blood sample at several time points to find out what happens to the study drug in the body called pharmacokinetics

The sponsor may have a representative present at the first enrolled patient's first dose at each site. Please ask the study doctor if you have any questions.

Treatment Visit 5
You will return to the clinic prior to your surgery for the following assessments:

- Computed tomography (CT) scan at a separate location: Norton Hospital Radiology
- Ask you how you are feeling
- Report any medication you have taken
- A physical exam that includes examination of your mouth and neck
- 12 lead ECG
- Tumor measurement and photographs

Safety Follow-up Visits at Months 1, 3 and 6 (Visits may also be scheduled to coincide with your standard of care visits)

- Ask you how you are feeling
- Report any medication you have taken
- A physical exam that includes examination of your mouth and neck
- Provide blood and urine samples for routine safety labs

The total amount of blood taken from the time of Screening through the Month 6 Follow-up Visit will be less than 1 cup. Additional blood (approximately 1-2 teaspoons each) may be collected if you have any adverse events or abnormal laboratory results that require repeating the tests.

What will happen when the study ends?
A final report will be provided to the study doctor who may share study results with you, if requested. The disclosure of published results will be available to all participants. You will not be identified by name in any of these reports.

What possible risks can I expect from taking part in this study?
In people who have ever been infected with hepatitis B virus, there is a risk that the virus can flare up during treatment with drugs that affect your immune system (such as chemotherapy). This could lead to liver failure or even death. This risk of hepatitis B virus flaring up may continue for several months after you stop taking these types of drugs.

You are to confirm at the baseline visit if you have or have ever had Hepatitis B, C and/or HIV and you will be excluded from the study if you have active disease and/or history of disease at any time prior to the screening visit. It is possible that you could be infected with hepatitis C, B and HIV with no symptoms. Therefore, it is your responsibility to confirm you do not have and have never tested positive for Hepatitis B, C and HIV.

State/Provincial law requires positive test results for certain communicable diseases, including HIV, hepatitis, sexually transmitted infections, and tuberculosis, to be reported to a local health agency. Some of the tests for this study must be reported when positive. The study doctor can discuss this with you.

This is the first time the PRV111 patch has been tested in humans, so there may be side effects that are not known. It has been tested in laboratory animals that were watched closely for up to 2 years. In animals that were treated with this patch, PRV111 did not show most of the bad and toxic side effects known to occur when the same chemotherapy (cisplatin) is administered intravenously (into the vein).

The study doctor will go through the risks associated with study participation prior to signing this informed consent form. You will be closely monitored. You should also talk to your study doctor about any side effects that you have while taking part in this study. Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect. The study doctor may be able to treat some side effects, or they may have to adjust the study treatment to try to reduce side effects. Some side effects caused by cisplatin may go away soon, some may last a long time, or some may never go away. Some side effects may be serious. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of PRV111 (Related to Cisplatin in Patch):

- Metallic taste
- Oral mucositis (inflammation of the lining cells in your mouth)
- Nausea and vomiting

Rare:

- Decrease in blood counts that may cause infection, bleeding, and bruising
- Loss of appetite
- Hearing loss or ringing in the ears
- Muscle cramps or spasms
- Loss of coordination while moving
- Involuntary movements or shaking
- Rash
- Vision problems
- Hair loss
- Low mineral levels in your blood
- Decrease in liver function causing temporary elevation in blood tests
- Loss of muscle or nerve function, which may cause weakness or numbness in your hands and feet
- Decreasing ability of the kidneys to handle the body's waste, which may be permanent
- Allergic reactions, which can cause difficulty in breathing, fast heartbeat, and sweating
- Acute myeloid leukemia

[redacted]

- [redacted]

Other Risks and Discomforts

Risks from blood draws and electrocardiograms:
Routine needle sticks for blood samples may cause pain, bruising, dizziness and rarely infection, at the site where blood is drawn. You may experience some minor irritation from the adhesive (sticky pads) used for the electrocardiograms.

Risks from CT scans and MRI:
CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel "closed in" while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. You may drink liquid to help define various organs. This may cause nausea and/or vomiting. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause flushing, nausea, and/or severe allergic reactions. It can damage your kidneys. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

During the MRI, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

Reproductive risks:
The effects of the study drug on an unborn baby are not known. If you are a woman, you should not become pregnant or breastfeed a baby while taking part in the study. You will be required to have a negative pregnancy test prior to the start of the study. If you are a man, you should not father a baby while taking part in the study.
Surface Prep Tool:
This will be used at the investigator's discretion prior to patch application and you may have bleeding, pain and/or infection from use of this surface prep tool.

It is important that you and your partner understand that you need to use birth control while in this study. If you are a female participant and become pregnant or the female partner of a male participant and become pregnant, you must tell the study doctor right away. The study doctor will notify the sponsor to discuss any follow-up with you.

Are there benefits to taking part in the study?
Taking part in this study may or may not make your health better. Toxicities related to pre-operative therapy could lead to delay in definitive potentially curative therapy (e.g., salvage surgery). The study will also provide knowledge toward more effective treatments for oral cancer patients. The information from this study will help researchers learn more about the effects of PRV111 as a treatment for oral cancer.

What are my other choices if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:

- You may choose to have radiotherapy alone, surgery with or without additional radiotherapy and/or chemotherapy, as this is the standard treatment;
- You may choose to take part in a different study, if one is available;
- Or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms. Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

Can I stop being in the study?
Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can complete follow-up tests for safety. This study visit will protect you from any unexpected side effects and will document your condition upon leaving the study.

Your participation may be discontinued without your consent by the study doctor, the sponsor or a regulatory agency for the following reasons:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow directions for taking part in the study
- If the study is cancelled

If you withdraw your consent during the study, personal information already collected will be retained to ensure the results of the study are measured properly. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the study results.

What are the costs of taking part in this study?
The costs for the PRV111 patches will be supplied at no charge while you take part in this study. You or your insurance company/third party payer will be billed for all routine procedures and the cost of treating injuries resulting from routine procedures. Routine procedures and drugs are those that you would likely receive whether or not you are in this study. You will be responsible for any deductibles or co-payments that are associated with your insurance coverage.

Will I receive compensation for my participation?
All Subjects:

To compensate you for time and expenses for participating in this study, you may receive a $50 stipend at the end of each of the following study visits: Screening, Visit 1, Visit 2, Visit 3 and Visit 4 to cover parking and travel costs. The total amount you can receive is $250.

Non-Local Subjects:
If you travel to a visit, the study sponsor may reimburse you for study-related travel costs and/or expenses. Study staff will review the reimbursement plan with you at the beginning of the study to see if you qualify.

1. Mileage at the standard rate of ($0.59/mile) plus any tolls incurred.
2. Reimbursement for a reasonable public transportation method (including bus, train, Uber, Lyft, or taxi) up to $100.00/day.
3. Meals may also be reimbursed (up to $50.00/day) and lodging (not to exceed $150.00/night).

Payments will be made to you on a prepaid debit card. Payments will be loaded onto your card within one day of your visit.

If you receive compensation for being a part of this research study, you may be asked to complete a W-9 tax form to report the compensation to the Internal Revenue Service. The amount you receive will count as income and may affect your income taxes. Your social security number will be required to complete the W-9 tax form.

What if I am injured from participating in the study?
If you think that you have been hurt by taking part in this research, [redacted] (24 hours), as soon as possible. If needed, emergency medical care will be provided. If the injury is a direct result of a study-related procedure or because you are taking PRV111 patch, the cost of the emergency medical care will be paid by the sponsor. The Sponsor has no plans to pay for medical care for any other injury whether or not it might be related to taking part in this research.

You voluntarily consent to take part in this study. If you feel that you have been injured as a result of being in this study, you should immediately contact the study doctor. The study doctor will treat you or will refer you for treatment.

If the study doctor and sponsor determine that the injury is a direct result of receiving the study drug or the properly conducted study procedures due to your participation in the study, and you have followed the study doctor's instructions, the sponsor will reimburse you for any reasonable cost of emergency and/or acute medical care you received for treatment. Injury that is the direct result of effects of receiving the study drug or the properly conducted study procedures due to your participation in the study does not include any underlying pre-existing medical condition. Other compensation, such as for lost wages, disability or discomfort, is not available.

Be aware that your health care payer/insurer might not cover the costs of study-related injuries or illnesses.

If you are injured as a result of this study, you do not give up your right to pursue a claim through the legal system.

Confidentiality:
Your privacy is very important and the study staff will make every effort to protect it. Your identity and records throughout the study will be kept as confidential as possible in accordance with applicable law. All of your test results and medical reports will be identified by a unique code and the list that links the code to your name will be kept separate from your tests and medical reports. The list will not be sent to the sponsor, Privo Technologies.

Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

Other groups may need to look at your medical records and study forms to make sure that the information is correct and to evaluate the conduct of this research study. These include the following:

- The sponsor of this study, Privo Technologies
- Western IRB, a group of people who review the research with the goal of protecting the people who take part in the study.
- Regulatory agencies in the United States, such as the Food and Drug Administration (FDA), Department of Health and Human Services and the Office for Human Research Protections
- The University of Cincinnati

A federal regulation known as the Privacy Rule gives you certain rights concerning the privacy of your health information. Researchers covered by this regulation are required to get your authorization (permission) to use and disclose (share with others) any health information that could identify you. You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you.

If you sign this informed consent form, you are giving permission for the use and disclosure of your health information for purposes of this research study. You do not have to give this permission. Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form. However, if you do not sign this form, you will not be able to participate in the study.

Who Will Use and Disclose My Health Information? The study doctor and research staff (the study team) may use your health information to conduct, review, and determine the results of the study. The study team may also use your information to prepare reports or publications about the study. However, your name will not appear in any report or publication without your permission.

What Health Information will be Used and Disclosed? The study team will record your medical history, the treatment you receive, and the results of examinations and tests done during the study on study forms. The study team will send the completed study forms to the study sponsor. Representatives from the groups identified below may need to look at your medical records to make sure that the information on the study forms is correct or that the study was conducted properly. Your medical records may include other health information about you and may include documents that directly identify you. Reviews like that will take place at the study center or where the medical records are stored and can take place after the study is over.

Who Will Receive My Health Information? Your study information or medical records (as described above) or both may be shared with the following people or groups:

- The study sponsor or its representatives, including companies it hires to provide study-related services
- Researchers who are conducting this study at other study centers
- Institutional Review Board and any other committees responsible for overseeing the research
- Staff of [redacted]
- [redacted] employees providing service or care to you
- Federal and State agencies, such as the U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS), the National Institutes of Health (NIH), and other US and non-US government bodies that oversee or review research

Will My Information be Protected by the Privacy Rule After it is Disclosed to Others? [redacted] required by the Privacy Rule to protect your health information. After your information is shared with others, such as the study sponsor, it may no longer be protected by the Privacy Rule. The people who receive this information could use it in ways not discussed in this form and could disclose it to others. The sponsor will use and disclose your information only for research or regulatory purposes or to prepare research publications. In addition to using it for this study, the sponsor may reanalyze the study data at a later date or combine your information with information from other studies for research purposes not directly related to this study. The goal of any such research would be to learn more about drugs or diseases or to help design better studies in the future. When using your information in these ways, the sponsor may share it with regulatory authorities, other researchers, its business partners, or companies it hires to provide research-related services.

What Happens if I Leave the Study Early? If you stop participating in the study early for any reason, the study team will tell the sponsor why. If the study team asks you to come to any more study visits and you agree, the study team will send the sponsor information from those visits as well. All information collected about you may continue to be used and disclosed.

Will My Authorization Ever Expire? This Authorization does not have an expiration date. The study team may need to correct or provide missing information about you even after your study participation is over and a review of your medical records may also take place after the study is over.

May I Take Back My Authorization? You have the right to take back (revoke) your Authorization at any time by writing to the person in charge of this research study whose information is listed on the front of this form. If you revoke your Authorization, the study team will not collect any new health information about you. However, they can continue to use and disclose any already-collected information if that is necessary for the reliability of the study. The sponsor can also still keep and use any information that it has already received. If you revoke your Authorization, you can no longer continue to participate in the study.

May I Look At My Study Information? You have a right to see and make copies of your medical records. However, to ensure the reliability of the study, you will need to wait to see your study records until the study is completed.

Who can answer my questions about the study?
You can talk to the study doctor about any questions, complaints, or concerns on this study or to report side effects or injuries.

Contact the study doctor [redacted] (24 hours). Please call if you:

- Think the research has hurt you.
- Have general questions about giving consent or your rights as a research participant in this research study.
- Have questions, concerns, suggestions and/or complaints about the research.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (800) 562-4789, help@wirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

To report complaints or concerns to an independent agency in an anonymous and confidential manner, please call the Research Compliance Hotline at 1-800-889-1547.

Use of Tissue and Blood for Research: Consent Form

About Using Tissue and Blood for Research:
After you complete study treatment, you will have surgery as part of your oral cancer treatment. Your doctor will remove the cancer tissue. The tissue removed during the surgery will be microscopically examined by a pathologist. The pathologist will check the tissue specimen and tell the status of your cancer, the number of viable tumor cells in the specimen and other parameters of the cancer and the margins. Your surgical specimen will also be tested for the level

of some cancer marker levels. The results of these tests will be given to you by your doctor and will be used to plan your care.

You will sign a separate consent form before the surgery. This will be a standard surgical consent form from the institution where the surgery and pathological sample will take place.

We would like to keep some of the tissue that is left over for future research. The samples will be labeled with a code number. To ensure your privacy, your name and information will not appear on these samples. If you agree, this tissue will be kept and may be used in research between us and our research collaborators to learn more about cancer and other diseases. Please read the information sheet called "Providing Your Tissue for Research: What You Need to Know" to learn more about tissue research. This information sheet is available to all at the following web site: https://www.cancer.gov/publications/patient-education/providing-tissue.pdf.

As a result of your participation in the trial, you also will have blood tests performed before you start treatment, during and at completion of your treatment. We would like to keep for future research about 3 tablespoons of the blood taken at that time. If you agree, this blood will be kept and may be used in research to learn more about cancer and other diseases.

The research that may be done with your tissue and blood is not designed specifically just to help you. It might help people who have cancer and other diseases in the future. Reports about future 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.

Old tissue Samples:
A biopsy (pathology samples) or tissue block from your oral cancer has been taken, at the time you were diagnosed with oral cancer. It's important for the researchers to evaluate and compare your initial biopsy (that was obtained before the study treatment) with the cancer tissue obtained during your surgery. We seek permission to look at older biopsy samples and tissue blocks.

Things to Think About:
We appreciate the use of tissue and blood for cancer research but the choice is yours to allow us to keep them for future research. 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 and let us know of your decision by contacting us. As the result, any tissue and blood that remain will no longer be used for research. In the future, people who do research may need to know more about your health. While the Doctor/institution may give them reports about your health, he/she will not provide your name, address, phone number, or any other information that can identify you.

Benefits:
The benefits of researchers using tissue and blood include learning more about causes of different cancers and developing ways to prevent or 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 very unlikely.

Making Your Choice:
Please read each sentence below and think about your choice. After reading each sentence, check "Yes" or "No". If you have any questions, please talk to your clinician or nurse.

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

1. My specimens may be kept for use in research to learn about, prevent, or treat cancer, as follows:
- Tissue Yes No
- Blood Yes No

2. Someone may contact me in the future to ask me to take part in more research.
Yes No

3. I agree that data (Samples/reports) regarding my old pathology tissue samples will be used for research aims.
Yes No

You will get a copy of this form. If you want more information about this study, ask your study doctor.

Consent and Signature

I have read or someone has read to me, this Informed Consent Document which describes the purpose and nature of this research. I have had time to review this information and have been encouraged to ask questions. If I do not participate or if I discontinue my participation, I will not lose any benefits or any legal rights. My participation in this research is completely voluntary. I have received (or will receive) a copy of this signed and dated form for my records and future reference. I have been given the information about the use and disclosure of my health information for this research study. I give my consent to participate.

_____
Subject Name (printed)

_____ _____ _____
Signature of Subject Date Time

_____
Name of Person Obtaining Informed Consent

_____ _____
Signature of Person Obtaining Informed Consent Date