Official Title: Smoking Cessation in Patients With Squamous Cell Cancer of the Head and Neck Undergoing Radiation Therapy With or Without Chemotherapy
NCT02582008
IRB-Approved Date: 7/18/2018

Section of Hematology and Oncology

SMOKING CESSATION IN PATIENTS WITH SQUAMOUS CELL CANCER OF THE HEAD AND NECK UNDERGOING RADIATION THERAPY WITH OR WITHOUT CHEMOTHERAPY

Informed Consent Form to Participate in Research
Mercedes Porosnicu, MD, Principal Investigator

INTRODUCTION

This is a clinical trial, a type of research study. Your doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your doctor for to explain any words or information contained in this informed consent document that you do not understand.

You are being asked to take part in this study because you are an active smoker (smoked within the last 30 days), have been diagnosed with a cancer of the head and neck, and are scheduled to receive radiation therapy as part of your treatment.

WHY IS THIS STUDY BEING DONE?

Patients with head and neck cancer undergoing radiation therapy with or without chemotherapy are first faced with the diagnosis of cancer and then with important changes to their daily life that can take an emotional toll on patients. It is estimated that 84% of head and neck cancer patients smoking at the time of their diagnosis will quit smoking without any specialized help, but unfortunately about 60% of patients will re-start smoking after treatment finishes. It is so important for your health to be able to not smoke again and we want to see if there are treatments that are better than others to help you not re-start smoking. Many patients feel anxious and depressed while taking treatment for their head and neck cancer and later while recovering from treatment. We want to compare a medication that can also help with depression signs called bupropion (Zyban®) with other treatments known to help patients to stop smoking and to prevent from re-starting smoking. All medications used in this study are approved by FDA as strategies to help with quitting smoking.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

60 people at 2 research sites will take part in this study, including approximately 30-40 people at this research site.

WHAT IS INVOLVED IN THE STUDY?

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in any group.

Arm A: Treatment with bupropion to help you to stop smoking
Arm B: Choice of treatment with Varenicline (Chantix®) or with a nicotine patch plus (if needed) short-acting nicotine replacement therapy (such as lozenges or gum) to help you to stop smoking

No matter which medication you are being randomized to take to help you quit smoking, we want to make you aware that there are nicotine withdrawal symptoms so you know what to expect. You will have the same risk of developing these symptoms even if you decide to quit without any medical help:

	Frequency of occurrence
Anxiety	88%
Irritability	80%
Difficulty concentrating	73%
Restlessness	71%
Tobacco craving	62%
Gastrointestinal problems	33%
Headaches	24%
Drowsiness	22%

All study –related treatment and interventions will occur with your usual clinic visits, so you will not be scheduled for any additional visits to our clinics.

Treatment Administration:

Treatment will start before beginning your treatment for head and neck cancer. We will establish a quit date as soon as possible and ideally 2 or more weeks prior to planned surgery or radiation therapy as continued smoking increases risk of complications.

If you are randomized to treatment with bupropion, you will be started at 150 mg/day for three days, then 150 mg twice a day thereafter while on this study protocol, for up to 1 year. Long acting bupropion tablets (that you take just once a day) are preferred. However, whenever needed (difficulties with swallowing pills due to trouble swallowing or sore throat) short acting bupropion will replace the long-acting pills in the same dose. Short- acting pills can be crushed and swallowed or given through a PEG tube. You will be instructed how to do this.

If you are randomized to the second arm to take a medication other than bupropion, you will

review with your physician the options and make a decision based on your medical history, risks, previous quitting attempts and your preference.
The two choices are:
A) Varenicline (1 mg daily during the first week, followed by 1 mg twice daily for 12 treatment weeks) or
B) combination of nicotine patch with possible use of other nicotine replacement medications as needed (such as gums, lozenges, inhaler, spray), also for 12 weeks. Patch dose will be dependent upon heaviness of smoking and generally is set to 21 mg for first 8 weeks, followed by 14 mg for 2 weeks, and 7 mg for 2 weeks. The dosage for the other nicotine replacement medications will be 4 mg throughout the treatment period.
C) If you refuse both Varenicline and nicotine patches you will be offered nicotine lozenges or gum or inhaler or spray as needed.

While being on this study you will be asked to keep a diary about taking the treatment to help you stop smoking and about the number of cigarettes that you smoke every day. You will review this diary with your doctors or other members of the study team at each visit. You will complete a brief smoking questionnaire. At each clinic visit, counseling and support will be available to you from members of the study team to answer your questions regarding smoking, medications, how they can help you quit smoking, and not re-start smoking.

If you are randomized to treatments other than bupropion and you have difficulties quitting smoking on current medications or if you quit but re-start smoking, we will offer you a longer duration treatment beyond the initially planned 12 weeks, we will talk to you about increasing the dose (if on nicotine patch) or add another treatment method.

Other tests and procedures:

If you take part in this study the following tests and procedures will occur prior to starting your cancer treatment at week 4 of your radiation treatment, the end of your radiation treatment, and then 3, 6, and 12 months after your radiation treatment has ended:

- Blood test: approximately half of a teaspoon of blood will be collected from you in addition to your regular blood drawn for your cancer treatment. This order will test for presence of nicotine in your blood. For this additional test, the total amount of blood withdrawn will be approximately 4 teaspoons.
- Exhaled carbon monoxide test. The smoking of tobacco, particularly as cigarettes, results in increased levels of carbon monoxide in your breath and in your blood. The level of the carbon monoxide in the breath is approximately equivalent with the level in the blood. The level can be measured using an exhaled carbon monoxide monitor. Exhaled carbon monoxide test is a non-invasive test that involves holding your breath for 20 seconds and then blowing into the monitor, which then provides a measurement. Within a few seconds, the digital readout shows the level of carbon monoxide in the breath that is a reflection of the level present in the blood. This test will be used instead of the blood test described above only for the patients treated with nicotine patches or other nicotine products while on the treatment with these medications because the blood test result can

appear like you are smoking even when you are not, while you are under treatment with medications containing nicotine.

- At the same visits when we will test your blood for nicotine we will ask you to complete questionnaires, that are lists of questions regarding your smoking situation, anxiety, depression, and complaints that you have from treatment that affect you and your well-being.
- During the treatment with radiation and in the two weeks immediately after treatment we will collect information on the amount of inflammation and pain that you have in your mouth and throat.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study prior to starting treatment and, for the duration of treatment in the treatment arm which is 12 weeks and the overall duration for about 12 months after you finish your radiation treatment.

Can I Stop Participating In The Study?

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about how this can affect your risk to continue to smoke and to start smoking again and the consequences for your general health and for the cancer to come back from continuing to smoke.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. These risks are the risks of the treatment that helps you stop smoking and not starting to smoke again. It is considered that the risk of these medications is smaller than the risk of continued smoking. You should discuss the risk of being in this study with the study staff.

Here are important points about how you and the study doctor can make side effects less of a problem:

- 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.
- The study doctor may adjust the study drugs to try to reduce side effects.

Tell your doctor if you have history of serious hypersensitivity reactions or skin reactions to bupropion, Varenicline, or nicotine medications.

If you are taking Bupropion or Varenicline we ask you to immediately report any worsening of your sadness or anxiety, unusual thoughts or thoughts about killing yourself. If you have any seizure activity inform your doctor immediately and stop taking the treatment.
As part of this study, you will be asked questions about your feelings, behavior and thoughts. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities.

If you are randomized to taking Bupropion possible side effects can include:

Common

- Tachycardia (elevated heart rate) risk 11%
- Weight gain risk 2-9%, Weight loss risk 14-19%
- Abdominal pain risk 2-9%, Constipation risk 5-10%, Nausea risk 13-18%, Xerostomia (dryness of mouth) risk 17-26%
- Confusion risk 8%, Dizziness risk 6-11%, Headache risk 25-34%, Insomnia (sleeplessness) risk 11-20%
- Agitation (anxious or nervous) risk 2% to 9%
- Nasopharyngitis inflammation of sinuses) (seasonal affective disorder) risk 13%, Pharyngitis risk 3-11% , Upper respiratory infection (seasonal affective disorder) risk 9%.

Serious but rare:

- **Cardiovascular:** Complete atrioventricular block (heart blockage), Myocardial infarction (heart attack)
- **Gastrointestinal:** Colitis (inflammation of colon), Pancreatitis (inflammation of pancreas)
- **Hematologic:** Pancytopenia
- **Hepatic:** Abnormal liver function, Hepatitis, Jaundice, Liver damage
- **Immunologic:** Anaphylactoid (allergic) reaction, Anaphylaxis (life threatening allergic reaction), Delayed hypersensitivity disorder
- **Musculoskeletal:** Rhabdomyolysis
- **Neurologic:** Seizure (risk of 0.1-0.4%)
- **Psychiatric:** Delusional disorder, Depression, Hallucinations, Hostile behavior (risk of 6%), Hypomania, Mania (a mild degree of abnormally elated mental state), Precipitation of episode, Paranoid ideation (an exaggerated, sometimes grandiose, belief or suspicion, usually not of a delusional nature, that one is being harassed, persecuted, or treated unfairly), Psychotic disorder, Activation, Suicidal behavior, Suicidal thoughts
- **Respiratory:** Pulmonary embolism (obstruction of a blood vessel in the lungs, usually due to a blood clot, which blocks a coronary artery)
- **Other:** Angioedema (rapid swelling of the deep layers of the skin)

Avoid consumption of alcohol while taking the Bupropion because this can increase your risk of side-effects.

If you are randomized to taking medications other than Bupropion and you and your doctor choose to take Varenicline, these are the possible side effects from this drug:

Common

- Constipation risk 5-8% , Flatulence risk 6-9%, Nausea risk 30%, Vomiting risk 5-11%
- Dream disorder risk 9-13%, Headache risk 11-19%, Insomnia risk 10-19%

Serious but rare:

- **Cardiovascular:** Angina risk 2.3% , Myocardial infarction risk 2%
- **Neurologic:** Cerebrovascular accident (cerebral stroke)
- **Ophthalmic:** Acquired night blindness (rare), Blurred vision (infrequent), Retinal vascular disorder (rare), Subcapsular cataract (rare), Transient blindness (rare), Visual disturbance (infrequent)
- **Psychiatric:** Abnormal behavior, Depression risk 3.5% to 11%, Hostile behavior risk 2%, Mood disorder risk 2.3%, Suicidal behavior, and/or ideation risk 6% to 11%

If you are randomized to taking medications other than Bupropion and you and your doctor chose to take nicotine patches and/ or other nicotine replacement medications (lozenges, gum, inhaler, spray) you can have the following side effects:

Common

- Skin irritation if using the patch
- Nasal irritation if using a nasal spray or oral irritation with the inhaler
- Diarrhea, Indigestion, oral irritation for lozenges and gums
- Other: Nicotine withdrawal, Dizziness, headache, insomnia

Serious

- **Cardiovascular:** Cardiac dysrhythmia (rare) (abnormality in the rate, regularity, or sequence of cardiac activation.), Hypertension (rare) (high blood pressure), Tachyarrhythmia (rare) (an excessively rapid heartbeat accompanied by variation from the normal rhythm)
- **Immunologic:** Hypersensitivity reaction (rare)

There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Reproductive Risks and other Issues to Participating in Research

Pregnant women are excluded from participation in this study. Bupropion has been assigned a pregnancy category C, Varenicline has been assigned a pregnancy category C, and nicotine replacement products have been assigned to pregnancy category C (nicotine gum) and category D (transdermal patches, inhalers, and spray nicotine products) by the FDA. (Category C

pregnancy - Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.) Cigarette smoking is known to cause spontaneous abortion, low birth weight, and increased perinatal mortality, probably due to nicotine and carbon monoxide. Nicotine has been shown to cause adverse fetal outcome in animals when administered in high doses. The use of Bupropion, Varenicline, and nicotine replacement products are only recommended for use during pregnancy when the benefit outweighs risk, noting the possibility the patient may continue to smoke while using these products.

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Smoking has been associated with poorer treatment results in patients with head and neck cancer, including surgery complications, a lower rate of response to radiation therapy and platinum-based chemotherapy. Smoking has also been associated with higher risk of cancer coming back, cancer-related death and death due to other causes, as well as an increased risk for other cancers to develop in the head and neck or lungs area. The benefits of participating in this study may be to help you to stop smoking, and not to start smoking again after treatment is complete. It also might help you to cope better with your treatment and treatment complications with lower levels of depression and anxiety. Because individuals respond differently to treatment, no one can know in advance if the treatment that we prescribe to you will be helpful in your particular case.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment to help you stop smoking. The same medications are available for you outside of this study. You should talk to your doctor about all the choices you have.

What About My Health Information?

By taking part in this research study, your personal health information, as well as information that directly identifies you, may be used and disclosed. Information that identifies you includes, but is not limited to, such things as your name, address, telephone number, and date of birth. Your personal health information includes all information about you which is collected or created during the study for research purposes. It also includes your personal health information that is related to this study and that is maintained in your medical records at this institution and at other places such as other hospitals and clinics where you may have received medical care. Examples of your personal health information include your health history, how you respond to

study activities or procedures, laboratory and other test results, and information from study visits, surveys, and physical examinations.

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information.

Because this research study involves the diagnosis and treatment of smoking, the Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Porosnicu that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Mercedes Porosnicu, MD

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but

any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. 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 Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

WHAT ARE THE COSTS?

Taking part in this study may lead to added costs to you or your insurance company. We will give you an estimate of what the added cost may be based on your particular situation and insurance coverage.

WILL YOU BE PAID FOR PARTICIPATING?

Parking validation will be provided for all study-related visits. You will receive no payment or other compensation aside from parking validation for taking part in this study.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University Health Science. The researchers do not hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this

coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Mercedes Porosnicu at 336-713-5440.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Mercedes Porosnicu at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm