THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

Consent Revision Date: 09/02/2014

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Varenicline and Combined NRT for Initial Smoking Cessation and Rescue Treatment in Smokers: A Randomized Pilot Trial
2014-0213

Subtitle: Project Switch Pilot

Study Chair: Paul Cinciripini

1.

Participant's Name	Medical Record Number

You are being asked to take part in this clinical research study at The University of Texas MD Anderson Cancer Center ("MD Anderson"). This consent and authorization form explains why this research study is being done and what your role will be if you choose to take part. This form also describes the possible risks connected with being in this study. After reviewing this information with the person responsible for your enrollment, you should know enough to be able to make an informed decision on whether you want to take part in the study.

You are being asked to take part in this study because you are a smoker and interested in treatment that may help you quit smoking or reduce the amount you smoke.

2. PURPOSE OF STUDY

The goal of this clinical research study is to test 2 therapies that may help people quit smoking. Researchers want to find out if one is more effective than the other. The 2 therapies are Chantix (varenicline) and a combination of a nicotine patch and nicotine lozenge. For participants who are still smoking after 6 weeks, the researchers also want to learn if it is better to continue with the same therapy or change the therapy.

3. DESCRIPTION OF STUDY

Screening Tests (Visit 0)
Signing the informed consent document does not mean that you will be able to take part in this study. You will have the following screening tests to help the doctor decide if you are eligible:

- You will be asked about your history of smoking and tobacco use, as well as alcohol and other drug use.
- You will complete questionnaires about depression, emotions, negative events, suicide, and your dependence on smoking. These questionnaires should take about 30 minutes total to complete.
- Your carbon monoxide (CO) level will be measured. CO is a gas that is found in higher levels among cigarette smokers. For this test, you will be asked to blow air through a CO-measuring device.
- Blood (about 2 teaspoons) will be drawn to check your liver and kidney function.
- If you can become pregnant, you will have a urine pregnancy test. To take part in this study, you must not be pregnant.
- Urine will be collected for a drug test. If the drug test is positive for marijuana, cocaine, opiates, benzodiazepines, barbiturates, amphetamines, methamphetamines, methadone, or PCP, screening will be stopped and you can be rescheduled to test again if you like. If you test positive a second time, you will not be able to take part in the study. The results will not be given to authorities. Please let staff know if you have a valid prescription for a medication that may cause you to fail the drug test.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

The study staff will give you letters recommending that you follow up with your primary care doctor if they think that follow-up is needed based on the information you provide during the screening visits or at any point during the study.

Study Groups

Weeks 1-6
If you are found to be eligible to take part in this study, you will be randomly assigned (as in a roll of dice) to 1 of 2 study groups. This is done because no one knows if one study group is better, the same, or worse than the other group. You will have an equal chance of being assigned to either group.

- If you are in **Group 1**, you will receive varenicline.
- If you are in **Group 2**, you will receive nicotine patches and lozenges.

Weeks 7-12
If you have quit smoking, you will stay in the group you were assigned to during the first 6 weeks of the study.

If you have not quit smoking, after 6 weeks in the study, you will again be randomly assigned (as in a roll of dice) to 1 of 3 new study groups. You will have an equal chance of being assigned to Groups 3, 4, or 5.

- If you are in **Group 3**, you will continue on the same drug (varenicline or nicotine patch/lozenges) that you were assigned at the beginning of the study.
- If you are in **Group 4**, you will switch to the patch and lozenges if you were receiving varenicline, and to varenicline if you were receiving the patch and lozenges.
- If you are in **Group 5**, you will receive an extra dose of the same drug that you were assigned at the beginning of the study, so you will take 1 extra dose of varenicline or apply 1 extra nicotine patch each day.

Study Drug Administration
You will start taking your assigned study drug(s) on **Day 9** (the day after Visit 1).

You should take **varenicline** tablets by mouth with a cup (8 ounces) of water after eating a full meal.

You should apply the **nicotine patch** to the upper arm. You should put it in a slightly different place each day to avoid skin irritation. You may take the patch off at night to avoid problems sleeping.

You may take the **nicotine lozenges** as needed throughout the day.

You will be given a study diary to record how many cigarettes you smoke (if any) each day while you are on study.

You must return your study diary and any unused study drugs, patches, lozenges, and/or containers at each study visit.

Weeks 1-6

Group 1
On **Days 9-11**, you will take 1 dose of varenicline each morning. Starting on **Day 12**, and then every day after that, you will take 1 dose in the morning and 1 dose in the evening (for a total of 2 doses of the study drug each day).

Group 2
Starting on **Day 12**, and then every day after that, you will apply 1 patch each day. You will also take nicotine lozenges as needed for cravings.

Study Visits

At **every study visit** (Days 8, 17, 24, 38, 52, 59, and 73):

- You will complete questionnaires about several topics, including depression, suicide, your smoking behavior, and any effects from the study drug. These questionnaires should take about 30-45 minutes in total to complete.
- You will receive counseling about quitting smoking, where you will talk about possible "triggers" for smoking and strategies for dealing with quitting smoking. These sessions will take about 15 minutes each.

At **Visits 1 and 5** (Days 8 and 52):

- Saliva will be collected for a routine test to check your cotinine levels. Cotinine is a chemical released in your body when it breaks down nicotine and will show whether and how much you have recently smoked.
- Your CO level and weight will be measured.
- At Visit 1 only, you will have a physical exam.
- If you can become pregnant, urine will be collected for a pregnancy test.

During your first counseling session (Visit 1), you will set a "quit date" for stopping smoking for about 1 week after you start taking the study drug. You should not quit smoking before the quit date. You may also set goals to reduce smoking. You will also be given a drug instruction sheet, a card with emergency contact information, and a participant manual to help you follow along with the topics discussed during counseling.

Some of the counseling sessions may be recorded by video and/or audio tape. The tapes will be used to make sure that the counselors are following the correct procedures and will be erased within 1 year after you complete the study. Your name and other identifying information will not be used. People that may be given permission to view and/or hear the tapes include study staff and faculty that review and rate how well the study counselors follow guidelines, and/or consultants that review how well the sessions are performed.

Visits 2, 3, 4, 6, and 7 (on Days 17, 24, 38, 59, and 73) will be done over the phone. You will complete questionnaires about several topics, including depression, mood, your smoking behavior, and any effects from the study drug. You will also be asked about any drugs you may be taking. Each call should take about 25-45 minutes.

The study staff will call you 1 day before your quit date and 3 days after your quit date to check on your progress in quitting smoking. Each call should take about 10-15 minutes.

Length of Study
You will receive the study drug tablets, patches, and lozenges for up to 12 weeks. You will be taken off study early if the doctor thinks it is in your best interest or if you are unable to follow study directions.

Your participation on the study will be over after the follow-up visits.

End-of-Treatment Visit (Visit 8/Day 94):
After you have finished taking the study drug, the following tests and procedures will be performed:

- Your CO level and weight will be measured.
- Blood (about 2 teaspoons) will be drawn to check your liver and kidney function.
- Saliva will be collected to measure your cotinine level.
- You will complete the same questionnaires you completed at the regular study visits.
- You will receive counseling about quitting smoking.
- If you can become pregnant, urine will be collected for a pregnancy test.

Follow-Up Visits (Visits 9 and 10):
At about 3 and 6 months after you have stopped smoking, the following tests and procedures will be performed:

- Your CO level and weight will be measured.
- Saliva will be collected to measure your cotinine level.
- You will complete the same questionnaires you completed at the regular study visits.

Other Information

- You must not take a type of drug called monoamine oxidase inhibitors (MAOIs, a type of antidepressant), drugs to quit smoking, or varenicline from another source while taking part in this study.
- You must tell the study staff about any drugs, including over-the-counter drugs, pain relievers, antacids, and/or herbal drugs you are taking or are planning to take during the study.
- The study drug must be kept out of the reach of children or others with limited ability to read or understand.
- Do not stop taking the study drug all at once unless you have an emergency or if you are told to do so by the study staff.

This is an investigational study. Varenicline, the nicotine patch, and the nicotine lozenge are FDA approved and commercially available to help people stop smoking. The study doctor can explain how the study drugs are designed to work.

The varenicline, nicotine patches, and/or nicotine lozenges will be provided at no cost to you while you are on study.

Up to 10 participants will take part in this portion of the study. All will be enrolled at MD Anderson.

4. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug and procedures.

Side Effects of Quitting Smoking

• slow heart rate • depressed mood • difficulty sleeping • irritability	• frustration • anger • anxiety • difficulty concentrating	• restlessness • worsening of existing mental illness • increased appetite • weight gain

Nicotine Patch Side Effects

It is not known how often the following side effects may occur.

• high blood pressure • fast heartbeat • difficulty concentrating	• swollen tongue • dry mouth • mouth blisters/sores (possible difficulty	• abnormal sensation (such as pins and needles) • hiccups

• depression • dizziness • headache • difficulty sleeping • nervousness • skin rash • sweating • increased saliva • bleeding gums	swallowing) • abnormal taste • constipation • gas • diarrhea • upset stomach • nausea • pain (joint/muscle/jaw)	• cough • infection • allergic reaction • application site reaction (such as skin rash, redness, swelling, and/or irritation)

To lower the risk of skin reactions, you should put the patch on a different skin area each day. To lower the risk of difficulty sleeping and abnormal dreams, you can remove the patch when you are sleeping and put on a new patch in the morning. To avoid possible burns, you should also remove the patch before having any magnetic resonance imaging (MRI) procedures.

Keep the patches out of the reach of children and pets. Unused and used patches have enough nicotine to poison children and pets. Be sure to fold the sticky ends together when you are done using the patch. In case of accidental overdose, call your doctor or a poison control center right away.

Nicotine Lozenge Side Effects

It is not known how often the side effects of the nicotine lozenge may occur.

• difficulty concentrating • depression • dizziness • headache • difficulty sleeping • nervousness • abnormal dreams • pain • application site reaction • swelling • skin redness and/or rash	• mouth sores • constipation • diarrhea • upset stomach • gas • bleeding gums • tongue inflammation • dry mouth • hiccups • jaw pain • nausea	• increased salivation • changes in taste • tooth problems • canker sore • joint and/or muscle pain • tickling/tingling sensation • cough • sinus inflammation • allergic reaction • sweating • increased blood pressure

Varenicline Side Effects

Common (occurring in more than 20% of patients)

• nausea

Occasional (occurring in 3-20% of patients)

• chest pain (possibly due to heart trouble) • headache • abnormal dreams • fatigue/lack of energy	• sleep disorder (possible difficulty sleeping) • skin rash • dry mouth • abnormal taste • increased appetite	• gas • constipation • abdominal pain • upset stomach • vomiting • infection

Rare but serious (occurring in fewer than 3% of patients)

• irregular, fast, and/or slow heartbeat • heart attack • decreased blood supply to the heart • heart and lung failure • blood clots in a vein and/or artery (possible pain, swelling, redness, and/or organ damage such as stroke and/or heart attack) • blood vessel disease or worsening of existing blood vessel disease • tissue swelling • dizziness • fever • multiple sclerosis (disorder of the central nervous system, causing motor difficulties) • seizure	• psychosis and/or delusions (loss of contact with reality) • murderous thoughts • paranoia (feeling of fear and/or mistrust) • suicidal thoughts, behavior, and/or attempts • changes in behavior • depression • aggression • agitation and/or anxiety • fainting • mood disorder with extremes of happiness and sadness • red, dry, scaly patches of thickened skin (psoriasis) • very severe blistering skin disease	• intestinal blockage • enlarged spleen • stomach ulcer • diarrhea • digestive system bleeding • gall bladder disease • inability to urinate • low blood counts (red, platelets) • trouble with balance • blind spots • temporary blindness • blurry vision • cataracts (clouding of the lens of the eye) • eye blood vessel disorder or other eye disorder • ear disorder that affects balance and

• stroke or temporary stroke symptoms • dizziness • paralysis (face) • loss of consciousness • mental and physical changes (such as memory loss and impaired thinking) • accidental injury • difficulty forming or speaking words • hallucinations (seeing or hearing things that are not there)	(with ulcers of the skin and digestive tract) • low blood sugar • diabetes • inflammation of the pancreas (possible abdominal pain) • thyroid disease • high blood levels of fat (possible heart disease and/or stroke) • low blood levels of potassium (possible weakness and/or muscle cramps)	hearing • deafness • kidney failure • difficulty breathing (possibly due to narrowing of the airways) • blood clots in the lung (possible failure to breathe) • allergic reaction (possibly affecting the skin)

Varenicline may rarely cause low blood cell counts (red blood cells and/or platelets).

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.

People who are taking varenicline and experience any serious and unusual changes in mood or behavior or who feel like hurting themselves or someone else should stop taking the medicine and call their healthcare professional right away.

Do not drive or operate heavy machinery until you know how varenicline affects you.

Other Risks
Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns after completing the questionnaires, you are encouraged to contact your doctor or the study chair.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

4a. Because taking part in this study can result in risks to an unborn or breastfeeding baby, you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you can become pregnant, you must use birth control while on this study. Acceptable forms of birth control include:

- hormonal contraceptives (such as birth control pills, patches, implants or injections)
- barrier methods (such as a condom or diaphragm used with a spermicide)
- intrauterine device (IUD).

Emergency contraceptives are not acceptable methods for routine use.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may result in your removal from this study.

5. POTENTIAL BENEFITS

Receiving varenicline, the nicotine patches/lozenges, and/or counseling may help you to quit smoking or change your smoking behavior. Future smokers may benefit from what is learned. There may be no benefits for you in this study.

6. ALTERNATIVE PROCEDURES OR TREATMENTS

You may choose not to take part in this study. You may choose to quit smoking without any help or with the help of nicotine replacement therapy products (such as the patch or lozenge) or other drugs. You may choose to receive varenicline and/or counseling outside the study as standard care. You may choose to receive other investigational therapy, if available. You may choose not to quit smoking. In all cases, you will receive appropriate medical care.

Additional Information

7. You may ask the study chair any questions you have about this study. You may contact the study chair, Dr. Paul Cinciripini, at 713-792-0919. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-2933 with any questions that have to do with this study or your rights as a study participant.

8. Your participation in this research study is strictly voluntary. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

9. This study or your participation in it may be changed or stopped at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP - a regulatory agency that oversees research in humans), or the IRB of MD Anderson.

10. You will be informed of any new findings that might affect your willingness to continue taking part in the study.

11. MD Anderson may benefit from your participation and/or what is learned in this study.

STUDY COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-2933 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs, including hospitalization, nausea, vomiting, low blood cell counts, and dehydration. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research. You may be compensated up to $480 plus parking vouchers or metro cards (if available) for completing all visits and assessments. You may receive partial payment for incomplete visits. You may receive compensation for the following visits:

$80.00 at Visits 5 and 10
$70.00 at Visit 1
$50.00 at Visits 8 and 9
$25.00 at Visits 0, 2, 3, 4, 6, and 7

Compensation will only be paid out at Visits 0 (Baseline), 1, 5, 8, 9, and 10. You will receive compensation for all applicable visits completed before each of these "payment" visits.

If a payment visit is missed, compensation for any completed visits will be given at the next payment visit. If you are more than 15 minutes late to a visit, $10.00 may be deducted from the allowable compensation for that particular visit. You must come to MD Anderson to receive compensation.

Authorization for Use and Disclosure of Protected Health Information:

A. During the course of this study, the research team at MD Anderson will be collecting and using your protected health information. This information may include personal identifying information about you (such as your name, race, date of birth, gender, city, and zip code), your medical history, study schedule, and the results of any of your tests, therapies, and/or procedures. The purpose of collecting and sharing this information is to learn about how the study procedures may affect the disease and any study-related side effects. Your doctor and the research team may share your study information with the parties named in Section D below.

   Quest Diagnostics will receive and analyze your blood samples.

B. Signing this consent and authorization form is optional. However, if you refuse to provide your authorization to use and disclose your protected health information for this study, you will not be able to participate in this research project.

C. MD Anderson will take appropriate steps to keep your protected health information private when possible, and it will be protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and it may be re-disclosed at some point. Federal agencies (such as the FDA, OHRP, or National Cancer Institute [NCI]), and the IRB of MD Anderson might view or receive your record in order to collect data and/or meet legal, ethical, research, and safety-related obligations. In some situations, the FDA could be required to reveal the names of participants.

D. Your protected health information may be shared with the following parties:

- Pfizer and NAL Pharmaceutical
- Federal agencies that require reporting of clinical study data (such as the FDA, NCI, and OHRP)
- The IRB of MD Anderson
- Officials of MD Anderson
- Study monitors who verify the accuracy of the information
- Individuals who put all the study information together in report form

E. Normally you have a right to access your medical record. However, in order to preserve the integrity of this research study, you will not be permitted to have access to certain portions of your medical record while the study is ongoing.

F. There is no expiration date for the use of your protected health information. You may withdraw your authorization to share your protected health information at any time in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP). You may contact the IRB Staff at 713-792-2933 with questions about how to find the NPP. If you withdraw your authorization, you will be removed from the study, and the study chair and staff will no longer use or disclose your protected health information in connection with this study, unless the study chair or staff needs to use or disclose some of your research-related personal health information to preserve the scientific value of the study. Data collected about you up to the time you withdrew will be used and included in the data analysis. The parties listed in Section D above may use and disclose any study data that were collected before you canceled your authorization.

G. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF PARTICIPANT _____ DATE _____

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF LAR _____ DATE _____

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

RELATIONSHIP TO PARTICIPANT _____

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2014-0213**.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) _____ DATE _____

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

PERSON OBTAINING CONSENT

I have discussed this clinical research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF STUDY CHAIR OR PERSON AUTHORIZED TO OBTAIN CONSENT _____ DATE _____

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into _____ and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

NAME OF TRANSLATOR	SIGNATURE OF TRANSLATOR	DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

SAMPLE -- NOT FOR USE IN CONSENTING PATIENTS

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR)	DATE