A Randomized Controlled Trial of Varenicline for Adolescent Smoking Cessation

NCT01509547

Informed Consent Form

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Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT
A Randomized Controlled Trial of Varenicline for Adolescent Smoking Cessation

If participants include those under 18 years of age: 1) The subject's parent or legal guardian will be present when the informed consent form is provided. 2) The subject will be able to participate only if the parent or legal guardian provides permission and the adolescent (age 12-17) provides his/her assent. 3) In statements below, the word "you" refers to your child or adolescent who is being asked to participate in the study.

A. PURPOSE AND BACKGROUND:

You are being asked to volunteer for a research study. This research is sponsored by the National Institute on Drug Abuse. The purpose of this study is to examine the effectiveness of varenicline, compared with placebo (a pill with no active medication), for smoking cessation (quitting smoking) in adolescent smokers and to examine the safety and tolerability of varenicline, compared with placebo, when used for smoking cessation in adolescent smokers.

You are being asked to participate in this study because you are a smoker aged 14-21. The investigator in charge of this study is Dr. Kevin M. Gray. This study is being done at the Medical University of South Carolina and will involve approximately 240 volunteers.

B. PROCEDURES:

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

1. Initial assessment: You will be asked to complete a variety of self-report forms about smoking and how you are feeling. A psychiatric evaluation will be completed, and urine will be collected for laboratory tests (urine drug screen, urine pregnancy test for females, and urine cotinine) to determine if you are able to participate in the study. For females, the urine pregnancy test will be done before any other testing, including the urine drug screen. If the pregnancy test is positive you will not be eligible to participate in the study and no further study procedures will be conducted. You may also be asked to provide a saliva sample to be measured for cotinine. A study medical clinician (either a study doctor or a physician assistant) will also do a brief physical exam to make sure you are healthy. This will include checking your vital signs, like your blood pressure, heart rate, height, and weight. We will also do a breathalyzer test, where you will blow into a machine, to determine your recent smoking status. Parents/guardians of participants under 18 years old will participate in the screening, evaluation, and informed consent/assent procedure.

During this visit, you will be given smoking cessation brochures and briefly counseled on strategies to help you quit smoking. You will be instructed to set a quit date that will occur one week after you start taking the study medication.

The research team will use several methods of contact to keep in touch with you. We will ask you to provide us with phone numbers, e-mail addresses, current home and work addresses, and contact

information of family and friends who may know how best to reach you. We will also have a Facebook account that we may use to contact you. The research team will only use private messages to contact you through Facebook.

2. Randomization (week 0): Once you complete the initial assessment and we determine that you are eligible for participation, you will be randomized to double blind varenicline or placebo and will proceed with treatment. There will be two treatment groups. One group will receive varenicline, the active medication and the other group will receive a placebo, a pill with no active medication. Volunteers will be randomly assigned to one of the two groups, which means that you have a 50/50 chance (like flipping a coin) of being assigned to either treatment group. Neither the researchers nor you will make the choice of which group to which you are assigned. Also, neither the researchers nor you will know which group you have been assigned.

3. Treatment (weeks 1 – 12): Once you are randomized to one of the two treatment groups you will receive either study medication or placebo (depending on your treatment group) in a blister pack that will include instructions on how and when to take the pills. You will be given a 7-day supply of medication to take home and an additional 7-day supply, which is a replacement pack of medication for use in the event that you cannot make your next scheduled appointment.

During treatment with the study medication you will be scheduled for weekly visits to see the study medical clinician, who will ask you questions about how you are feeling, including any side effects you may be experiencing.

You will be asked to keep study logs to keep track of the amount of medication you are taking each day. You will also be asked to keep a record of the amount of cigarettes you are smoking each day and if you are drinking any alcohol or using any drugs.

During the weekly visits, study personnel will review medication logs, inspect blister packs, and perform pill counts to monitor the amount of medication you are taking. You will also complete questionnaires about cravings, withdrawal, and satisfaction. Over the course of the 12 weeks you will also have periodic visits that will include additional medication safety and tolerability assessments.

At the weekly visits, you will be provided with brief (less than 10 minutes) individual counseling to help you quit smoking.

4. Post-Treatment Follow-Up (weeks 13 – 26): You will be asked to come in for 3 follow-up visits once you've completed taking the study medication. One visit will be scheduled one week after you have stopped taking the study medication, the second visit will be scheduled 6 weeks after you stop the study medication and the final visit will be scheduled 14 weeks after stopping the study medication. During these visits the study doctor will ask you about any side effects you may have. You will also complete several self-report forms, similar to the ones you completed at other study visits. We will collect a urine sample at the final study visit for a urine drug screen and a urine cotinine test. Female participants will have a urine pregnancy test at the week 13 follow-up visit

prior to the urine drug screen. If the pregnancy test is positive, the urine drug screen will not be performed. You may also be asked to provide a saliva sample to be measured for cotinine.

You may be withdrawn from the study without your consent if the researchers believe it is in your best interest or if you fail to follow study procedures.

C. DURATION:

Participation in the study will take about 28 weeks with a total of 17 visits. The first should last about 2 hours and remaining visits should last about 30 minutes – 1 hour.

D. RISKS/DISCOMFORTS:

1. Varenicline: If you are in the group that receives varenicline, the following side effects are possible: The most common adverse reactions were nausea (upset stomach), abnormal (e.g., vivid, unusual, or strange) dreams, constipation, flatulence, vomiting, and headache. In a 2-week adolescent varenicline pharmacokinetic study, the most common adverse events were nausea, headache, vomiting, and dizziness.

   There are no published reports on the safety and efficacy of varenicline in adolescents. More than 15 million adults have taken varenicline since it was made available as a prescription drug. **Since this time, there have been post-marketing reports of neuropsychiatric symptoms, some serious. In other words, after varenicline was approved by the FDA, symptoms related to mental health and nervous system functioning were reported by those who used it. These symptoms include:**

   - Changes in mood
   - Agitation (irritation)
   - Psychosis (mental disorder impairing thoughts/beliefs)
   - Hallucinations (seeing or hearing things not real)
   - Paranoia (feelings of suspicion)
   - Delusions (false notions/beliefs)
   - Homicidal ideation (thoughts of harming others)
   - Hostility (aggression)
   - Changes in behavior
   - Anxiety (worry)
   - Panic (fear)
   - Suicidal ideation (thoughts of killing self)
   - Suicide attempt (attempting to kill self)
   - Completed suicide (suicide resulting in death)

The above neuropsychiatric symptoms occurred in patients attempting to quit smoking with varenicline. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish causal relationship to drug exposure.

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If you have cardiovascular disease (heart or blood vessel problems), taking varenicline may increase your risk of certain cardiovascular adverse events. Contact the study doctor if you experience new or worsening symptoms of cardiovascular disease while taking varenicline, for example:

- Shortness of breath or trouble breathing
- New or worsening chest pain
- New or worsening pain in legs when walking

Smoking cessation with or without treatment is associated with nicotine withdrawal symptoms and the exacerbation of underlying psychiatric illness (i.e., worsening of existing illness). Not all patients had known pre-existing psychiatric illness and not all had discontinued smoking. The role of varenicline in these reports is not known.

You should stop taking study medication and immediately report any such symptoms to the study staff, and be sure to make known any history of psychiatric illness prior to beginning treatment.

2. Randomization: You will be assigned to a treatment program by chance. The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.
3. Placebo: If you are in the group that receives placebo, your condition will go without active treatment for 12 weeks.
4. If you are or become pregnant and test positive for illegal drugs, it is a law that the South Carolina Department of Social Services (DSS) must be notified. You and your family will be evaluated by the agency. You could be ordered to mandatory drug treatment, lose custody of your children, or possibly be jailed.
5. Unknown Risks: The experimental treatments may have unknown side effects. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.
6. Loss of confidentiality: Any communication of personal information carries the potential risk of loss of confidentiality.

E. BENEFITS:

The potential benefit to you is that the treatment you receive may prove to be more effective than the other study treatment or than other available treatments, although this cannot be guaranteed.

If you are in the group that receives varenicline and it proves to treat your condition with fewer side effects than the current standard therapy, you may benefit from participating in the study; however, this cannot be guaranteed.

F. COSTS:
You will not be charged for any of the study treatments or procedures. The costs of the study medication, all tests associated with this study, and all office visits will be covered by the study.

F. PAYMENT TO PARTICIPANTS:
You will receive compensation upon completion of each visit, according to the schedule in the table below.

Compensation schedule

Visit	Assessment	Wk 0	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8	Wk 9	Wk 10	Wk 11	Wk 12	Wk 13	Wk 18	Wk 26
Compensation ($)	$40	$40	$30	$30	$30	$40	$30	$30	$30	$40	$30	$30	$30	$50	$30	$30	$50
Maximum Possible Grand Total $590																	

If you receive $600 or more from MUSC (including cash, checks, gift cards or other gifts) during the calendar year, you will receive a tax Form 1099 and the IRS will be notified of the amount you received.

You are also invited to participate in the recruitment of other participants for this study. If you choose to participate, we will provide you with coupons that you may give to other people (e.g., peers, acquaintances) who you think would be eligible and interested in this study. You may choose to tell people to whom you give these coupons to call the study team if they are interested in participating in the study. These individuals will not be identified unless they contact the study office themselves. If any of your coupons result in successful scheduling and completion of a screening visit, you will receive $10 for each one. If that person is enrolled in the study (i.e. is eligible for the study and returns for the Week 0 visit), you will earn an additional $10. Participation in this process is completely voluntary, and if you elect not to participate your participation in this study will not be affected in any way.

G. ALTERNATIVES:
If you choose not to participate in this study, you could receive other treatments for your condition. Other treatments are available to help adolescents quit smoking include smoking cessation counseling**.** Your study doctor will discuss with you the major risks and benefits of the standard of care and alternative treatment option(s).

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

I. STUDENT PARAGRAPH: Your participation or discontinuance will not constitute an element of your academic performance nor will it be a part of your academic record at this Institution. The Charleston County School District nor any school that is a part of this district is neither sponsoring nor conducting this research. There is no penalty for not participating. Participants

may withdraw from the study at any time without penalty.

J. EMPLOYEE PARTICIPATION: Your participation or discontinuance will not constitute an element of your job performance or evaluation nor will it be a part of your personnel record at this Institution.

K. CONFIDENTIALITY CERTIFICATE:

A Certificate of Confidentiality has been obtained from the Federal Government for this study to help insure your privacy. This certificate means that researchers cannot be forced to tell people who are not connected with the study, including courts, about your participation, without your written consent. If we see something that would immediately endanger you, your child, or others, we may discuss it with you, if possible, or seek help.

L. DISCLOSURE OF PREGNANCY TESTING RESULTS OF FEMALES AGED 17 YEARS AND YOUNGER:

During your participation in this study, you will be given a pregnancy test. If you are under 16 years of age, the results will be shared with your parents and/or legal guardian.

If you are 16 years or older, you have the right to direct that such test results not be shared with your parents or legal guardian. Please initial in the space below to indicate your choice. Your choice will not affect your ability to participate in this research project:

___ Yes, you may share my pregnancy test results with my parents or legal guardian.
___ No, you may not share my pregnancy test results with my parents or legal guardian.

M. INVITATION TO PARTICIPATE IN FUTURE STUDIES

From time to time we have other research studies for which you might be eligible. We are inviting you to allow us to contact you by phone, mail, or both to see if you would be interested in participating in any future studies. By checking the "yes" box below, you are indicating that you would like to give us your phone number, any alternate phone numbers, and address so that we may contact you if another study becomes available. To maintain your confidentiality, we will not leave identifiable messages or any identifiable information on letters or envelopes that are mailed to you. By checking the "no" box below, you are indicating that you do not want study personnel to contact you for any future studies. You may

still participate in the current study if you check "no" and you will not suffer any adverse consequences in doing so.

☐ Yes! I would like to be re-contacted for future studies. I give permission for study personnel to contact me by phone or by mail to inform me of other available studies I may be eligible for. Please initial here_____.

☐ No. I do not wish to be re-contacted for any future studies. Please initial here_____.

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. 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. Kevin Gray at 843-792-2123. I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment.

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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.
If you wish to participate, you should sign below.

Signature of Person Obtaining Consent	Date	*Name of Participant	Date

Signature of Adult Participant Date

Signature of Parent/Legal Guardian Date

*12-17 years of age:
"My participation has been explained to me, and all of my questions have been answered. I am willing to participate."

Signature: _____

Age: _____ Date of Birth: _____