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Title: New Treatment for Alcohol and Nicotine Dependence

Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

Principal Investigator:	Nassima Ait-Daoud Tiouririne, M.D. University of Virginia Center for Leading Edge Addiction Research 560 Ray C Hunt Drive Charlottesville, VA 22903 Tel: (434) 243-0570
Sponsor:	National Institute of Alcohol and Alcohol Abuse (NIAAA)

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a signed copy of this form.

Who is funding this study?

This study is being funded by a grant from the National Institute of Alcohol and Alcohol Abuse (NIAAA).

Why is this research being done?

In this study we are testing a drug called topiramate to see if it will help people who are addicted to alcohol and who smoke cigarettes, cut down on their number of heavy drinking days and help quit cigarette use. Topiramate was approved by the Food and Drug Administration (FDA) in December 1996 as a medication for all adults with partial onset seizures. This drug has not been approved by the FDA for the treatment of alcohol dependence or smoking cessation.

Over 12,500 adults and children have participated in J & JPRD-Sponsored Clinical Studies of Topiramate.

You are being asked to participate in this study because you have an alcohol dependence and also smoke cigarettes and have indicated a desire to stop drinking and quit smoking.

Up to 588 people will be in this study at all places. 196 people will be enrolled at UVa.

How long will this study take?

You will need to come in for a screening visit to make sure it is safe for you to be in the study. Screening procedures could take 4 to 6 hours and may be done over two or more visits. There are 15 study visits following the screening period. Each visit will last about 2 hours. There will also be a follow-up visit at one

month and a follow-up phone call at three months following the last treatment visit. Your participation in this study could take about 9 months to complete.

What will happen if you are in the study?

SCREENING (will take approximately 4-6 hours to complete):

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. Screening will take place at UVA's Center for Leading edge Addiction Research (UVA CLEAR). This office visit will take approximately 4-6 hours to complete. During screening we will determine if you are eligible and if it is safe for you to participate. The following will be performed at this visit:

- You will sign a separate consent that will ask you to blow into a small device (Breathalyzer) that will measure the amount of alcohol on your breath (BAC). This test must be $\leq$ 0.000 in order for you to continue participating.
- Review of your medical history and current medications you may be taking
- Physical exam and vital signs (blood pressure, heart rate, weight, breathing rate, temperature)
- Standard blood tests (multiple samples, a few tablespoons of blood) to make sure that your liver and kidneys and bone marrow work properly, as well as blood sugar levels
- Conduct a carbon monoxide (CO) test (CO is the colorless, odorless, tasteless gas that is created as a result of smoking cigarettes)
- Urine sample: The urine test will screen for drugs of abuse including cocaine and opiates (heroin, morphine, methadone, or codeine containing substances). If you are dependent on any other drugs besides alcohol and nicotine, you will not be eligible to participate in this study. Results of your urine tests will be placed in study records, which are confidential. Urine will also be collected for standard medical testing. Your urine will also be tested for cotinine level (Cotinine is created as a result of smoking cigarettes) if the result of your CO test is below certain levels.
- An electrocardiogram (ECG) to check cardiac electrical currents of the heart
- You will also be asked questions on your alcohol and cigarette use, sleeping habits and general well-being
- All females who are able to have children will take a urine pregnancy test that must be negative in order to continue study participation
- Collect a saliva sample to test the amount of cotinine in your saliva.

If these tests show you are eligible, you will return to the clinic (within 30 days) to begin study treatment.

RANDOMIZATION and STUDY TREATMENT

(15 visits and each visit will last about 2 hours):

You will be randomly assigned (like the flip of a coin) to 1 of 3 study treatment groups. Two out of 3 will receive the study drug. You have an equal chance of being assigned to any one of the groups. Neither you nor your doctor can choose which group you are assigned. Neither you nor your doctor will know which study treatment you will get until the study is done. But if your doctor needs to know, the people doing this study can find out.

GROUP 1: Low-dose topiramate (up to 125 mg/day)

GROUP 2: High-dose topiramate (up to 250 mg/day)

GROUP 3: Placebo

A placebo is a harmless substance that looks like the study drug, but which should have no effect.
**** For the purpose of this study, we will refer to both Topiramate and Placebo as the "study medication"**

All groups will receive treatment for a total of 18 weeks and will receive BBCET sessions (Brief Behavioral Compliance Enhancement Treatment) no matter which treatment you are assigned to.

All groups will also receive a self-help manual for smoking cessation.

During the first 10 weeks of the study, you will be asked to come for clinic visits once a week for about two hours. For weeks 10 to 18 you will be asked to come in once every 2 weeks and your last treatment visit will be at week 19.

You will be seen in person at the clinic for 14 visits (intervention phase-Visits 1-14). During these visits you will do the following:

- Attend a BBCET session
- Obtain your medication
- Fill out questionnaires and rating scales
- Conduct an alcohol breath test (BAC) and record your daily consumption of alcohol
- Conduct a carbon monoxide (CO) test (CO is the colorless, odorless, tasteless gas that is created as a result of smoking cigarettes) and record your daily cigarette use
- Have your vital signs taken

If you are a woman of child bearing potential you must provide a urine sample at various times throughout the study for a urine pregnancy test that must be negative in order to continue study participation.

Urine will also be collected at various times throughout the study to test for drugs in your body.
We will also test your urine sample for cotinine level at visit 1 if your CO test is below 10 ppm.

At your last study treatment visit (Visit 15) you will also be seen in person and will do the following:

- Attend a BBCET session
- Return any and all remaining study medication bottles
- Fill out questionnaires and rating scales.
- Conduct an alcohol breath test (BAC) and record your daily consumption of alcohol.
- Provide a blood sample
- Provide a urine sample
- Provide a saliva sample
- ECG
- Conduct a carbon monoxide (CO) test (CO is the colorless, odorless, tasteless gas that is created as a result of smoking cigarettes) and record your daily cigarette use

- Have your vital signs taken

During this study, you will be asked to fill out some questionnaires. These questionnaires ask about:

- how you are feeling
- your lifestyle habits
- medicine use
- diet
- daily activities
- family history
- how you feel about taking part in this study

These questionnaires will take about 15-20 minutes to complete.

At the beginning of each clinic visit, the amount of alcohol in your breath (BAC) will be measured using a breathalyzer and if it is greater than 0.020, you will be presented with three options. First, you are welcome to stay until the reading goes down. We will check your BAC once every hour until it is less than or equal to 0.020 for alcohol. At that point, depending on the schedule and time of the day, you can either continue with the visit or reschedule for another day. Second, we will offer the use of the telephone so you can arrange transportation from a friend or family. Third, if you are unable to find alternate transportation and you are unable to stay, we will provide transportation for you at no cost

FOLLOW UP:

At the end of the treatment period, you will be scheduled to attend a follow-up visit at 1 month after Visit 15. The 1-month follow-up visit will last about one hour. During this follow-up visit you will be given many of the same surveys that you completed throughout the first 19 weeks of the trial. We will also collect your carbon monoxide (CO) level and BAC at this visit.

You will also have a follow-up phone call at 3 months after Visit 15. During the 3-month follow-up, one of our staff members will call you. We will ask you about your cigarette and alcohol use and any alcohol withdrawal symptoms you might have experienced since the 1-month follow-up.

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- You will have to attend all study visits as scheduled
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Ensure that the study drug is taken as instructed, keep the study drug in a safe place away from other children, return any unused study drug at each visit, and report any lost or missed tablets.
- Ensure that the study drug is taken only by you, the person for whom it has been prescribed.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.

Study Schedule

Study Procedures	**Screen**																	
Study Treatment Week	-4 to -1	1	2	3	4	5	6	7	8	9	10	12	14	16	18	19	F/U 1 month	F/U 3 month (phone)
Visit Number	S	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Informed Consent	X																	
Breath Alcohol Content	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Vital signs and weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Physical Exam/ECG	X															X		
Record of Daily Alcohol Consumption and Cigarette Use	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review study eligibility	X	X																
Brief Behavioral Compliance Enhancement Treatment (BBCET)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Review of any health problems Adverse Event Checks	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Receive “Clearing the Air” Booklet		X																
Carbon Monoxide (CO) Level	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Urinary Cotinine Level	X	X																
Saliva Collection	X															X		
Urine Drug Screen	X							X						X		X		
Urine Pregnancy Tests	X	X			X			X			X			X		X		
Blood draw (for laboratory testing)	X															X		
Blood draw (for genotyping)	X																	
Self-administered Questionnaires	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Study Medication Dispensation		X	X	X	X	X	X	X	X	X	X	X	X	X	X			

Specimens

Blood testing
We will draw up to 3 tablespoons of blood at screening and visit 15. The total amount of blood we will take will be 6 tablespoons of blood for the entire study.

The blood we take will be tested to measure for the amount of red blood cells, the amount of white blood cells, how well your kidney and liver work, the amount of certain fats, salts and sugar in your body.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

Optional Collection of Health Information and Samples for Genetic Research and Specimen Banking

What Sort of Research Will Be Done On Your Sample(s)?
You are also being asked to provide samples of your blood to be used for research. Your sample might help doctors learn more about diseases or treatments that might help other people in the future.

We plan to do genetic research on the DNA in your specimen sample. DNA is the material that makes up your genes. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work, and determine physical characteristics such as hair and eye color. Genes are passed from parent to child.

In addition, if you agree, specimens collected for research will be added to a research specimen bank. The purpose of a specimen bank is to process, and store samples until researchers need them for future research. The long term goals of the samples collected in this bank will be mainly used for research related to alcohol use and smoking. It is not possible, however, to list every research project that will include the samples because we cannot predict all of the research questions that will be important over the coming years. As we learn more, new research questions and new types of research may be done.

What will you have to do to give samples for research?
If you agree to provide blood samples, no more than 2 tablespoons of blood will be drawn at the screening visit. This sample will be used to study your genes. If you provide us with samples for testing but you are later found to be excluded from the study, your samples will be tested nonetheless.

This part of the study is optional. You do not have to agree to donate your sample(s) in order to be in the first part of this study.

How Will Your Sample(s) Be Labeled?
Your sample(s) will not be labeled with your name or other information that would identify you directly.

Dr. Nassima Ait-Daoud Tiouririne will be responsible for storing your sample and for protecting your privacy. Your sample(s) will not be labeled with your name or other information that would identify you directly. Instead, it will have a unique code that allows for it to be linked to some of your health information. This link means that your specimen can be identified but only indirectly. We can find out if we need to know which sample is yours in the event you wish the sample to be removed at a later date.

Which researchers can use your samples and what information about you can they have?
Your sample may be shared with researchers at the University of Virginia and at other institutions. Dr. **Nassima Ait-Daoud Tiouririne** will not give your name to other researchers who want to use your sample, but will only give them information like your age and what disease/condition you have. Those who would see the information would include researchers and the others listed under "Who will see your private information?" section of this consent document.

Some of the people who receive your information may not have to follow the privacy laws and may share or release your information because they do not have to follow the privacy laws.

What Are the Benefits To Donating Your Sample(s) For Genetic Research and Specimen Banking?
The genetic research and specimen banking that is done with your sample is not meant to help you. But, doctors hope that in the future it will help people who have other diseases or conditions.

What Are The Risks of Donating Your Sample(s) For This Study?

<u>Risks to Privacy from Genetic Research:</u>
The main risk of allowing us to store and use your samples and certain limited health information for research is a potential loss of privacy. One of the risks to you is the release of information from your health records. The University of Virginia will do its best to protect your records so that facts about you and your health will be kept private. The chance that information identifying you will be given to someone else is very small. However, we cannot *guarantee* it will be safe. To further safeguard your privacy, information obtained from future research will not be placed in your medical record.

There are certain risks of having health information given to other people by mistake. In the unlikely event that this happens, it could cause discrimination or mental harm to you or your family members if others were to see this information. The results could be that you may not be able to get or keep certain kinds of insurance. It could also hurt family relationships.

Because everyone has unique DNA, it is also possible, although very unlikely, that someone could identify you through your DNA if they have another sample of your DNA.

Information about your genetic make-up could mean that you and your family members could face problems that could lead to getting or keeping some kinds of insurance or affect your ability to get or keep a job. To

keep this from happening, the results of these tests will not be given to anyone outside of the study staff. There is no way to predict all the possible risks of this research.

Community harm

Risks to People Belonging to Certain Ethnic or Cultural Groups

Discrimination may occur when people believe that a certain ethnic or cultural group has an increased genetic risk of a disease, disability, or addiction. Someone belonging to that group may become a social outcast. They may even suffer insurance or employment discrimination.

There is no way to predict all the possible risks of this research. Genetic research is always changing. We may learn of other physical, social, or psychological risks in the future.

Will You Find Out the Results of the Research on Your Sample(s) for Genetic Research and Specimen Banking?

Neither you, your health care provider**,** nor anyone in your family, will receive the results of any research done on your sample(s). The results will not be put in your health records. Therefore, results from any research done on your sample(s) will not affect your medical care. This helps protect you and other members of your family from harm that might be caused by this information.

What If You Change Your Mind About Donating Your Sample(s) for Genetic Research and Specimen Banking?

If you decide now that your sample(s) can be kept for genetic research and/or specimen banking, and later change your mind, you can simply withdraw the sample(s) at that time. To withdraw you will need to write to the Principal Investigator listed on the first page of this form. We will then destroy any of your tissue that has not already been used. However, if your sample has been used in genetic research, the information that we have learned will remain in the study, even if you withdraw. Unless you withdraw from the study, permission for researchers to use your tissue and to use and share your private health information for this study will never end.

Will You Be Paid For Donating Your Sample(s) for Genetic Research and Specimen Banking?

You will be paid $20 for donating your sample for genetic research by check. You should get your payment at the end of the visit after donating your sample. The income may be reported to the IRS as income.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

Will Donating Your Sample(s) Cost You Any Money?

There is no cost to you to have your samples collected or used for genetic research.

Genetic Testing:

You do not have to participate and agree for specimens to be collected for genetic research in order to be in the main part of this study. No matter what you decide to do, your decision will not affect your medical care. You can tell us your choice by placing your initials in one of the options below:

GENETIC RESEARCH:
Please indicate your choice by placing your initials below (if applicable):

___ YES **Your sample(s) may be used for genetic research**

___ NO **Your sample(s) may not be used for genetic research**

SPECIMEN BANKING:
Please indicate your choice by placing your initials below (if applicable):

___ YES **Your sample(s) may be saved for future research and stored in a specimen bank.**

___ NO **Your sample(s) may not be saved for future research and stored in a specimen bank.**

What are the risks of being in this study?

Risks and side effects related to topiramate include:

Likely

- sleepiness
- dizziness
- tiredness
- tingling of the skin
- slowed thinking and movement
- loss of appetite
- weight loss

Less Likely

- problems with coordination
- speech disorder and related speech problems
- confusion
- difficulty with memory
- difficulty concentrating
- change in sense of taste
- nervousness
- eye jumping
- depression and other mood problems
- nausea

Other rare side effects

Metabolic acidosis (decreased bicarbonate in the blood) may be associated with topiramate treatment. Metabolic acidosis can cause symptoms such as tiredness and loss of appetite, or more serious conditions including irregular heartbeat (arrhythmia) or coma. Long-term metabolic acidosis can result in thinning of the

bones (osteoporosis) with an increased risk for fractures. In children, this condition may reduce growth rates which may eventually decrease maximum height achieved. Metabolic acidosis may increase the risk for kidney stones.

Treatment with topiramate may cause decreased sweating (oligohidrosis), which has primarily been reported in pediatric patients. Activities such as exercise or exposure to warm temperatures while using topiramate may increase the risk of heat-related side effects, such as heat stroke. Drinking plenty of fluids while using topiramate is recommended.

A medical condition consisting of sudden worsening of vision and an elevation of fluid pressure in the eyes (acute secondary glaucoma) has been described in patients taking topiramate, usually occurring in the beginning of their treatment. If you have sudden, significant worsening of vision, blurred vision, or eye pain you should contact your study doctor immediately.
Rare and isolated cases of liver failure/hepatitis and blistering skin rashes (bullous skin eruptions) have been reported.

Topiramate may cause a change (increase or decrease) in the effect of some other medications. If you are taking other medications during your participation in this study, your doctor will explain whether topiramate may have an effect and if necessary, may adjust your medication dose.

Topiramate may reduce the effectiveness of some hormonal birth contraceptives (birth control pills, hormonal implants or hormonal injections) and additional barrier methods, such as condoms or a diaphragm, should be used. If you are taking birth control pills, you should report to your study doctor any change in your bleeding patterns. Rarely, increases levels of ammonia in the blood (hyperammonemia) with or without impairment of brain function have been reported with topiramate mainly when it was taken together with valproic acid.

Isolated reports of seizures associated with a rapid decrease of topiramate have occurred in patients with or without seizure disorders.

Recent reports of temporary loss of vision in patients treated with topiramate have been observed. To minimize the risk we will exclude all patients that have a history of glaucoma. You will be monitored during the study for unusual headaches, sudden blindness, and a feeling of pressure in the eyes.

IMPORTANT: The FDA recently looked at studies where patients had received antiepileptic drugs like topiramate. They found that the people in the studies they looked at were at about twice the risk for suicidal behavior or thoughts compared with patients receiving placebo. A placebo is a harmless substance that looks like the study drug, but has no effect.

During the research, if we learn you are having thoughts about suicide or hurting yourself or others, the research staff will ask you more questions about your thoughts. Based on your response, the staff may provide you with help to get treatment. This may include: working with you to contact your doctor or therapist,

referral to a therapist to discuss your thoughts, contact a trusted family member, significant other or clergy or work with you on a plan that may include getting you to a hospital for safety and treatment.

If you begin to have symptoms of depression (such as sadness, worthlessness, low energy) or have thoughts of suicide, call the clinic or study doctor immediately. If the clinic is closed, please call our 24-hour answering service at (434) 972-1974, or 911.

In clinical trials using Topiratmate, 11% of patients (this is 11 out of every 100 pateints) discontinued due to adverse events. Compared to placebo, 1% of patients treated with Topiramate (200-400 mg) had a greater incidence of adverse events. Most patients who experienced adverse events during the first 8-weeks of treatment, were no longer experiencing side effects at their last visit.

In addition, a total of 1.5% of patients (this is one out of approximately every 101 pateints) exposed to topiramate can develop kidney stones. The use of topiramate at the same time as other carbonic anhydrase inhibitors, such as acetazolamide and zonisamide, may increase the risk of kidney stone formation, and should therefore be avoided. Drinking plenty of liquids is recommended to reduce new stone formation. You should inform the study doctor of any medication you are currently taking and before taking any other medication. You will be monitored weekly for the occurrence of side effects and other potential difficulties associated with this treatment study.

There may be risks to topiramate that are now not known. You will be notified of any new significant findings that might affect your willingness to continue in the study.

Risks of Audio taping:

During each study visit, your brief, one-on-one session with a medical professional will be audio taped. Random samplings of these audio recordings are for quality control training. You will be asked to give additional authorization if you choose to participate in this audio taping.

By placing a check mark and initialing, I give my permission to be audio taped: _____

By placing a check mark and initialing, I DO NOT give my permission to be audio taped: _____

Risks from Placebo:

There is the risk that you will not get the study drug so your condition may get worse.

Risks from Completing Questionnaires:

Some of the questions about your personal habits, lifestyle, and drug and alcohol use may embarrass you. If any question makes you feel uncomfortable you may discuss its importance and the need to answer it with the specially trained interviewer. You may refuse to answer a question if it is upsetting to you.

Risks of Sharing the Drug

Do not share the study drug with anyone. It is prescribed only for you and could hurt someone else. Keep it out of reach of children and people not able to read or understand the label.

Blood Donation

If you participate in this study it may affect your ability to donate blood. If you have any questions call the organization where you donate blood and talk to one of their nurses.

Risks of having your blood drawn:

Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:

- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV or any other infection that may affect your clinical care, we will tell you the results and help you understand what the results mean for you.

Risks for women:

If you are pregnant now, or get pregnant during the study, please tell us. Being in this study might hurt your unborn baby, so you will not be able to join or stay in the study. Also, you should be sure you do not get pregnant for one week after the study. Use an effective method of birth control during this time. .Effective methods of birth control include but are not limited to oral contraceptives (birth control pills), hormonal implants, or barriers including condoms or diaphragms plus spermicidal foam cream or jelly. If you have questions about effective birth control, please ask the study leader.

Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

We cannot promise that you will be helped by being in this study. You may benefit from being in this study, however we cannot guarantee this. You will receive a check of your physical health, by our staff to ensure that you are in good physical condition. You will receive brief counseling for the treatment of alcohol dependence and cigarette use and you will receive a self-help guide for the treatment of your cigarette use. It is possible

that you will experience an improvement in your alcohol dependence and cigarette use as a result of participating in this study. You may also obtain some benefits from the medication. In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include

- Taking a medication approved by the FDA to treat alcohol dependence such as disulfiram (Antabuse), or naltrexone. However, in order to participate in this study you must necessarily delay this customary treatment.
- Taking a medication approved by the FDA to treat nicotine dependence such as varenicline, bupropion and nicotine replacement therapies such as: patch, gum, lozenge, inhaler or nasal spray.
- Other non-medication treatments like psychotherapy or joining a local chapter of Alcoholics Anonymous (AA) or Nicotine Anonymous (NA).

However, in order to participate in this study you must withhold or delay the usual treatment.

If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will receive $275.00 for participating and completing this study. You should expect to receive your payment by check after each visit.

You will be compensated $20.00 following your initial screen, $15.00 at completion of the requirements for each visit (15 visits), and $15 for each follow-up visit (2), so a total of $275.00. The income may be reported to the IRS as income.

If you owe money to the University of Virginia or the University of Virginia Medical Center, the money to be paid to you in this study can be withheld to pay what you owe. And if a court has issued a judgment against you, the money may also be withheld to pay the judgment creditor for such things as taxes, fines, or child support that you owe.

By agreeing to be in this study, you are donating your blood, and bodily fluids, for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance and include physical examinations, ECG's, blood and urine tests and study drug, which are required as part of the study procedures.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to return all study medications and complete the safety and research assessments that would have been completed during Visit 15.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth

- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.
- Tissue or blood samples if you agree to provide them for genetic testing for this study.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

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.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

We have asked the federal government to issue a Certificate of Confidentiality, to help protect the privacy of your study records. If we receive a subpoena or court order demanding information from the study records that would identify you, we will use the Certificate to resist the demand. However, UVa will not use it in the following cases.

- You have agreed in writing to allow UVa to share the information with your employer, your insurance company for billing purposes, or someone else

- Reports to authorities where there is a danger that you may harm yourself or others, or if there is evidence of probable child or elder abuse or neglect.

In addition, the Certificate does not prevent government authorities who oversee research from reviewing this study. This Certificate does not mean that the government either approves or disapproves of this study. It just helps protect your privacy

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Nassima Ait-Daoud Tiouririne, M.D.
University of Virginia
Center for Leading Edge Addiction Research
560 Ray C Hunt Drive
Charlottesville, VA 22903
Tel: (434) 243-0570

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Consent from Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE