

Title: Phase I Drug Interaction and Subjective Effects of Compounds for Opioid Use Disorder

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RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

TITLE: Phase I Drug Interaction and Subjective Effects of Compounds for Opioid Use Disorder

VCU IRB PROTOCOL NUMBER: HM20008062

INVESTIGATOR: Dr. F. Gerard Moeller

Study Sponsor: National Institute on Drug Abuse (NIDA)

If any information contained in this consent form is not clear, please ask the study doctor or the study staff to explain any information that you do not fully understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

INVITATION TO TAKE PART

You are invited to take part in a research project called “**Phase I Drug Interaction and Self Administration Studies of Compounds for Opioid Use Disorder**” conducted by Dr. F. Gerard Moeller, of Virginia Commonwealth University (VCU) School of Medicine. For this research project, he will be called the Principal Investigator or PI.

We are inviting you as a person who has been using opioids to take part in this clinical research study to look at the interaction between a medication (lorcaserin, trade name Belviiq) and opioids. At some point during the study you will be given an inactive placebo while at other points during the study you may be given lorcaserin. We ask you to please read this form carefully.

PURPOSE OF THE STUDY

The main purpose of this investigational study is to find out how the medication lorcaserin reacts with oxycodone and the effects of lorcaserin on how oxycodone makes a person feel. Lorcaserin is a medicine that is approved by the FDA for the treatment of obesity under the trade name Belviiq. Oxycodone is a medicine that is approved by the FDA for the treatment of pain under a variety of trade names including OxyContin and OxyIR. More information about how lorcaserin reacts with oxycodone may be helpful to develop new treatments for addiction to oxycodone and other opioids. The study will enroll a total of 72 people all at VCU.

PROCEDURES

If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered.

Your participation in this study will last up to 28 days (including intervening weekends).

You are either currently enrolled or have already completed the primary eligibility screening procedure as per the screening protocol (HM20000294) and have potentially

qualified to participate in this study . If needed, you may have up to 2 additional visits lasting approximately 1 hour each at CARI before your first hospital day in order to confirm study eligibility.

After you complete the screening, we will review the test results and tell you if you qualify for continued study participation. If you live more than 20 miles from VCU, you may stay overnight during the screening at a nearby hotel at no cost to you (we will make the hotel arrangements for you).

The study will consist of one hospital day at the Clinical Research Services (CRS) unit at VCU Medical Center, three days at the Collaborative Advanced Research Imaging (CARI) facility, and another hospital day at the CRS. There will also be two follow-up visits at the CARI facility. The first hospital visit at the CRS will last about 10 hours. After the first visit in the hospital you will have three visits at the CARI facility which will last around two hours each. The next day after the last visit to the CARI facility you will have a second hospital visit that will last about 10 hours, just like the first hospital visit. When you arrive at the CRS unit, you will be asked to shower and change into hospital scrubs. Your street clothes and personal belongings (including your cell phone), will be collected from you and stored in a secured area for safekeeping until you leave the unit. We ask that you leave any valuables at home prior to your CRS visit. Visitors will not be allowed during either of your hospital visits, and you must remain on the unit at all times during your visit. If you leave the unit before the end of the visit this will lead to you being dropped from the research study. VCU is a non- smoking campus, so no tobacco products will be allowed. If you are a tobacco user, we can provide you with a nicotine patch at a dose based on the amount of cigarettes you typically smoke per day.

During each hospital visit, you will be asked to provide a urine sample for complete drug screen analysis, and a breath sample to screen for alcohol. If you are a woman, you will also be asked to provide a urine sample for a pregnancy test. Before starting any of the study drug procedures, you will get a physical exam, a heart test (electrocardiogram (ECG)) where electrodes are placed on you to measure the electrical activity of your heart, and be placed on monitors to continuously measure your blood oxygen level. You will then have a catheter (tube) inserted in a vein in your arm. At each visit a total of 9 blood samples (4 mL each, which equals approximately 1 teaspoon) will be drawn from an arm vein in order to check the amount of medication in your blood. The maximum total amount of blood that will be drawn during this study will be no more than 124 mL, which equals approximately 8 tablespoons. During each visit, you will also be given three doses of oxycodone (by mouth) and one of the following study medications to take by mouth at 8:00 a.m.; lorcaserin (10 mg); or Placebo (inactive pill). You will complete some questionnaires that ask about things like recent drug and alcohol use, cravings, and your mood, whether you have had any self-harm thoughts, and whether you have experienced any side effects. You will also be asked to complete some computer tasks of memory and attention, and also a computer task on how the oxycodone makes you feel. You will also have some tests of how oxycodone affects pain responses, which will be measured by your placing your hand in a container of cold water. At the end of each hospital visit, you will have a test of your coordination and you will be provided transportation home by taxi.

On the days you come to the CARI facility you will be given a dose of lorcazerin (10 mg); or Placebo (inactive pill). You will be given a dose of medication to take in the evening when you are at home. The medication you receive will be assigned randomly; that means the decision is made “by chance”, like the flip of a coin. Using the active study medication or placebo will test whether the medication really works. Urine samples will also be tested daily for drugs, and breath samples to screen for alcohol. If you are a woman, your daily urine sample will also be used for a pregnancy test. You will also be asked to complete some forms about how you have been feeling and your mood.

You will be asked to complete two follow-up visits after the last visit to the hospital. The first visit will take place three days after your hospital stay has been completed, and the second visit will occur a week later. On each day, you will be asked to provide a urine sample for complete drug screen analysis, a blood sample for study drug analysis, and a breath sample to screen for alcohol. If you are a woman, your urine will also be used for a pregnancy test. You will get a physical exam, and will also

be asked to fill out forms about how you feel, whether you have had any self-harm thoughts, and whether you have experienced any side effects. At the end of the second follow-up visit, you will also meet with the study investigator for a brief discussion about your study participation, and final instructions prior to completing the study.

If you live more than 20 miles from VCU, hotel accommodations can be provided at no cost to you during each of your study visits (we will make hotel arrangements for you). You will also be provided meals, and transportation to and from the hospital each day.

TIME COMMITMENT

The study elements and time are (see table below for schedule of activities):

1. Additional screening If needed you may have up to 2 additional visits of about 1 hours each at CARI before your first hospital day in order to confirm that you are eligible to participate in the study.
2. Hospital Day 0 (about 10 hours total time for the this day)
3. Outpatient CARI days 1-3: (about 2 hours each visit)
4. Hospital Day 4 (about 10 hours total time for this day)
5. Outpatient CARI days 5 and 6: Follow-up visit to the CARI for final checkup and testing (about 2 hours each)

The total maximum number of hours is about 46 hours spread over a maximum of 28 days.

Schedule of Study Activities

Visit	Baseline Day 0 Week 1	Day 1 Week 2	Day 2 Week 2	Day 3 Week 2	Day 4 Week 2	Day 5 Week 2	Day 6 Week 3
Where	CRSU	CARI	CARI	CARI	CRSU	CARI	CARI
Time required	10 hours	2 hours	2 hours	2 hours	10 hours	2 hours	2 hours

Activities	Urine collection Vital signs Study drug dispensed Blood draws ECG Cold water test Memory tasks Choice Tasks Questionnaires	Urine collection Vital Signs Study drug dispensed Blood draws Questionnaires	Urine collection Vital signs Study drug dispensed Questionnaires	Urine collection Vital signs Study drug dispensed Questionnaires	Urine collection Vital signs Study drug dispensed Blood draws ECG Cold water test Memory tasks Choice Tasks Questionnaires	Follow-up for side effects Urine collection Vital signs Blood draws Questionnaires Choice Tasks	Follow-up for side effects Urine collection Vital signs & ECG Questionnaires
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RISKS AND DISCOMFORTS

There are two kinds of risks; one is physical and the other is psychological (mental). The most common side effects of lorcaserin include headache, dizziness, fatigue, nausea, dry mouth, drowsiness, and constipation. Possible but uncommon side effects of lorcaserin include: a prolonged (more than 4 hours) painful erection (priapism), dry mouth, flushed dry skin, increased hunger, increased thirst, increased urination, itching, redness or swelling of the eye or eyelid, loss of consciousness, severe skin rash or hives, stomachache, sweating, tingling of the hands or feet, trouble with breathing, trouble with

sleeping, vomiting, and unexplained weight loss.

The risks of combining oxycodone and lorcaserin have not been studied in humans, although a study in rats did not find any additional dangers in the dosages that will be used in this study from opioids alone. However, there are potentially unknown risks of combining these two medications including the theoretical possibility of symptoms of serotonin syndrome (fever, agitation, confusion, rapid heart rate and high blood pressure), although this has never been reported.

The most common side effects of oxycodone are constipation, nausea, stomach pain, loss of appetite, and vomiting, and other symptoms including somnolence (sleepiness), dizziness, itching, headache, dry mouth, sweating, and decreases in the ability to feel pain. Possible but uncommon side effects of oxycodone include low blood pressure, and loss of consciousness leading to reduced breathing, which can be dangerous if not treated. Since you currently use opioids, these side effects are less likely, but not impossible. Possible side effects will be monitored carefully through blood pressure and breathing monitoring and a form that you fill out each day. The risks of combining oxycodone and lorcaserin have not been studied in humans, although both oxycodone and lorcaserin are being prescribed and there are no reports of any interactions between these medications. However, there are potentially unknown risks of combining these two medications. You will be provided with copies of the package

inserts for both lorcaserin and oxycodone which contain detailed prescribing information and a complete listing of potential side effects. For additional information you can consult the FDA database online at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>.

In order to test effects of lorcaserin and oxycodone on pain, you will have several tests that involve placing your hand in a container of ice water. This may be uncomfortable but you can remove your hand from the water when it becomes too uncomfortable for you.

The possible psychological effects of lorcaserin and oxycodone are changes in mood or behavior. We will ask you about your mood during the study and you should tell us if you are having any changes in your mood or thoughts of self-harm. Some of these questions will be about drug and alcohol use, sex, possible mental health problems, legal problems, or your family. You may be uncomfortable because of some of the questions that are asked during the interviews, but you have the right to refuse to answer any questions. You may feel uncomfortable when providing blood and urine samples and breath tests. If you are a smoker, you may also feel uncomfortable not being able to smoke during your hospital stays. To help relieve any discomfort from nicotine withdrawal, we can provide you with a nicotine patch dosed based on the amount of cigarettes you smoke per day. A television will be available in your room for entertainment, and a telephone will also be available for local calls.

Risks of Cocaine exposure: Medical complications that have been reported with cocaine use include heart attack, rupture of major blood vessels, stroke, difficulty breathing, swelling, cessation of bowel function, and death. Cocaine is a potent sympathomimetic and has been associated with adverse cardiovascular events, including myocardial infarction and stroke, when taken illicitly.

Risks of Lorcaserin Combined with Cocaine

In a recent NIDA funded preclinical study (NIDA Study Report 1812-12132, Sep. 20, 2013), lorcaserin was administered to rodents in combination with cocaine without any significant toxicity.

However, at 5-fold higher doses (i.e., 25 mg/kg in rats, equivalent to 100 mg/day in humans – substantially beyond what is used illicitly), there are indications of increased sensitivity to cocaine-induced convulsions due to lorcaserin. The combination of lorcaserin and cocaine is currently being studied in our active study (HM20003768- Phase I drug interaction and self-administration studies of compounds for Cocaine Use Disorder COCUD), which has found no risks associated with combined lorcaserin and cocaine use to-date. Further, lorcaserin is FDA approved and widely marketed for the treatment of obesity, and no adverse events have been reported to the FDA regarding lorcaserin in conjunction with illicit cocaine use.

Risks of positive urine drug screen:

Possible psychological effects of the urine drug screen are that you may be uncomfortable because of a positive drug test. If known to employers or insurance

companies, the results of urine drug screen might affect a person's ability to obtain a job or health or life insurance. However, data is being collected only for research purposes. Your data will be identified by ID numbers assigned to you by our study staff (not names), and stored separately from medical records in a locked research area. All personal identifying information will be kept in password protected computer files. Access to all data will be limited to study personnel. A data and safety monitoring plan is established. To help us protect your

privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health (see Confidentiality section below).

Special note to women: Additional risks to an unborn child may exist with study medications. Therefore, pregnancy testing will be done every day during the study. Women of childbearing potential must not be pregnant or breast feeding, and if sexually active, must be using acceptable methods of birth control to be enrolled in the study.

Acceptable methods include:

- a) Oral contraceptives
- b) Barrier plus spermicide
- c) Hormonal or surgical implants

Special note to men: Because of possible unknown risks of the study medication on reproduction, male subjects will be advised during the study to use a condom when having sex.

Risks associated with having an ECG include: psychological discomfort in learning of a potential health condition and the potential for hair removal where the ECG lead is applied to the chest. Some individuals who have allergies to tape adhesive may have a mild allergic reaction to the ECG adhesive.

Risks associated with the blood draws: You may have some pain and a bruise when the blood is drawn and at the location on your arm where the IV is placed. You will have your IV catheter replaced every day hours. There is also a slight chance of infection.

You will be asked to leave the study if you do not follow the study rules or complete the requirements and fulfill your responsibilities to complete the study visits, give urine or breath samples, or complete forms. It may also be necessary for you to leave this study if you have other problems or illness during the study. If this happens, appropriate referrals will be given.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Authority to Request Protected Health Information

The following people and/or groups may request my Protected Health Information:

- Health Care Providers at the VCUHS
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards
- Principal Investigator and Research Staff
- Research Collaborators
- Institutional Review Boards
- Government/Health Agencies

- Others as Required by Law

Authority to Release Protected Health Information

The VCU Health System (VCUHS) may release the information identified in this authorization from my medical records and provide this information to:

- Health Care Providers at the VCUHS
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards
- Others as Required by Law
- Principal Investigator and Research Staff
- Research Collaborators
- Institutional Review Boards
- Government/Health Agencies

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Type of Information that may be Released

The following types of information may be used for the conduct of this research:

- Complete health record

Expiration of This Authorization

- This authorization will expire when the research study is closed, or there is no need to review, analyze and consider the data generated by the research project, whichever is later.
- This research study involves the use of a Data or Tissue Repository (bank) and will never expire.
- Other (specify):

Right to Revoke Authorization and Re-disclosure

You may change your mind and revoke (take back) the right to use your protected health

information at any time. Even if you revoke this Authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator, Dr. F. Gerard Moeller at 203 East Cary St., Suite 202, Richmond, VA 23219.

BENEFITS TO YOU AND OTHERS

The benefit you can expect as a result of taking part in this study is information regarding your physical and mental health status learned during the screening procedures. It is also possible that information will be learned about how lorcaserin affects how people feel about opioids, which may help develop new treatments for drug abuse in the future.

COSTS

All medical tests, hospital stays, and study drug will be offered at no cost to you.

PAYMENT FOR PARTICIPATION

You will be compensated \$25 for each of the 1-2 additional eligibility confirmation visits (if needed). You will be compensated \$150 for each of the 2 hospital days, and an additional \$20 for each of the visits at the CARI clinic between and after the hospital stays for a total of \$400 for two hospital days and 5 clinic visits. If you complete the entire study as per specified procedures, you will receive up to \$450 dollars. Payment will be dispensed as follows:

You will receive \$25 for each eligibility confirmation visit needed (up to 2), and compensated at the end of each visit.

You will receive \$50 for the first hospital stay right after you complete your first hospital day.

You will receive \$20 for each of the CARI clinic visits completed between hospital stays (up to \$100 total for completing all five visits),

After your second hospital stay you will receive \$100.

You will receive the final payment (\$150) after your final follow-up visit.

Participants traveling more than 20 miles to VCU will be reimbursed for their travel expenses (mileage only at the current VCU rate), and hotel accommodations. Meals will also be made available to all participants for each of the study visits if timing of your study visit would make it difficult for you to eat on your own.

All compensation will be provided in the form of cash and or checks (that will be mailed to you).

If you are dropped early or choose to withdrawal from the study before completing it, you will receive a prorated portion of the compensation, based on the study activities you completed. Total payments within one calendar year that exceed \$600 will require the University to annually report these payments to the IRS and you. This may require you to claim the money you receive for participation in this study as taxable income. VCU is required by federal law to collect your social security number. Your social security number will be kept confidential and will only be used to process payment.

If you receive payment for taking part in this study please be informed that you will be asked to complete a W-9 form that will be forwarded to the accounting department as a requirement by the Internal Revenue Service. You will also be issued a 1099-Misc form from this study for tax reporting purposes.

ALTERNATIVE TREATMENT

This study is not intended to treat any medical condition. The alternative to taking part in this study is to not take part.

CONFIDENTIALITY

It will be noted in your protected electronic medical record at VCU Health System that you are in this clinical trial. Information about the study including any medications

other than the study medications you may receive will be noted in the record. This information is protected just as any of your other medical records are protected. The name of the study medication will not be in the electronic medical record. It will be listed as an investigational medication.

Your research data will be identified by ID numbers, not names, and stored separately from medical records in a locked research area. All personal identifying information will be kept in password protected files and these files will be deleted at the end of 6 years. Other study records will be kept in a locked file cabinet for 6 years after the study ends and will be destroyed at that time. Access to research data will be limited to study personnel. A data and safety monitoring plan has been established.

VCU and the VCU Health System have established secure databases to help with monitoring and oversight of clinical research. Your information may be maintained in these databases but are only accessible to individuals working on this study or VCU/VCUHS officials who have access for specific research related tasks. Identifiable information in these are not released outside VCU unless stated in this consent or required by law. Personal information about you might be shared with or copied by authorized officials of the Federal Food and Drug Administration or the Department of Health and Human Services.

We will not tell anyone the answers you give us. But, if you tell us that you intend to hurt yourself or someone else, the law says that we have to let people in authority know so they can protect you and others.

To help us protect your privacy, we will obtain a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to give out information that would identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained.

The Certificate cannot be used to resist a demand for information from employees of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be given in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily giving information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold the information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances, child abuse, elder abuse, the intent to hurt self or others, or required reportable communicable diseases, such as HIV.

No one outside the research staff may call and get information about you. If you decide you would like copies of your medical test results, you may sign a form to release information to you or your physician. Only specific medical information, not research information, will be released.

You will not be personally identified in any reports or publications that may result from this study. Any personal information about you that is gathered during this study will remain confidential to every extent of the law.

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 any information that can identify you. At most the website will include a summary of the results. You can search this website at any time.

COMPENSATION FOR INJURY or ILLNESS

If you suffer any injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment and professional services will be available to you, just as they are to the community in general. You should report any injury to Dr. Moeller at (804) 828-3810 (daytime) or (804) 828-0951 (after hours emergency paging). You will not give up any of your legal rights by signing this consent form.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study.

To help avoid research-related injury or illness it is very important to follow all study directions.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your decision to take part is voluntary and you may refuse to take part, or choose to stop taking part, at any time. A decision not to take part or to stop being a part of the research project will not change the services that are available to you from the research clinic or Virginia Commonwealth University School of Medicine. You do not have to take part in this study to take part in other research studies in the clinic. Your decision to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

You may refuse to answer any questions asked or written on any forms, however answering some questions about your health and safety are necessary to take part in this study.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent. The reasons might include:

- the study doctor thinks it necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study;
- administrative reasons require your withdrawal.

QUESTIONS

The investigators of this study will be glad to answer any further questions at any time. In the event of problems due to this study you should report them to Dr. Moeller at (804)828-3810. If you would like to withdraw your permission to use blood or tissue samples, mail address for sending a letter notifying us to 203 East Cary Street, Suite 202, Richmond, VA 23219.

If you have general questions about your rights as a participant in this or any other research, you may contact:

Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 3000
P.O. Box 980568

Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number for general questions, concerns, or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at <http://www.research.vcu.edu/irb/volunteers.htm>.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

CONSENT

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered.

By signing this consent form, I have not waived any of the legal rights or benefits, to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form once I have agreed to participate.

Participant Name, (Printed)

Participant Signature

Date

Name of Person Conducting Informed Consent Discussion / Witness (Printed)

Signature of Person Conducting Informed Consent
Discussion / Witness

Date

Principal Investigator Signature (if different from above)

Date