Methylnaltrexone vs Naloxegol in the Treatment of Opioid-Induced Constipation

NCT03523520

April 19, 2020

Consent Form and HIPAA Authorization

for Participation in a Research Study

Investigator's Name: Kara B. Goddard, PharmD, BCPS
Project IRB #: 2011409 HS

Study Title: Methylnaltrexone versus Naloxegol in the Treatment of Opioid-Induced Constipation in the Emergency Department

We invite you to take part in this research study. This consent form tells you why we are doing the study, what will happen if you join the study, and other important information about the study.

Please take as much time as you need to read this consent form. You can discuss it with your family, friends, or doctor. If there is anything you do not understand, please ask us to explain. Then you can decide if you want to take part in the study or not.

The Principal Investigator (also called the study doctor) is Kara Goddard, PharmD. The people working with Dr. Goddard on this study are called the study team.

What Should I Know Before I Decide Whether To take part In This Study?

- Research studies like this one help us to learn new things and test new ideas about treating certain conditions/diseases.
- Taking part in a research study is voluntary. You decide if you want to take part, and you can stop taking part at any time. Your regular medical care at the University of Missouri Hospitals and Clinics will not be affected now or in the future if you decide you do not want to be in this study.
- We are doing this study because we want to know more about the effectiveness of the medications approved to treat constipation caused by opioid medications (like oxycodone).
- We invite you to take part in this study because you are seeking treatment in our Emergency Department for constipation from an opioid pain medication.
- If you take part in this study, you will receive one of 3 study drugs, all of which are FDA approved to treat constipation caused by opioid medications.

- At the end of the study period, your regular medical care will continue and address any further pain or health concerns.
- About 60 people will take part in this study at the University of Missouri.
- The total amount of time you could be in this study is about 60 minutes.
- **There is no guarantee that taking part in this research will result in any improvement in your condition.**
- As with any research study, there are risks that we know about and there may be some we don't know about. We will explain these risks in this form.
- We will only include you in this study if you give us your permission first by signing this consent form.

Why Are The Researchers Doing This Study?

In this study, we want to find out if one medication used to treat constipation caused by opioids works better than another. To do this, we will compare two doses of methylnaltrexone (12mg subcutaneous injection and 450mg oral tablets) and naloxegol (25mg oral tablet) in people with constipation caused by opioids to see which one is more effective at treating constipation.

All three medications and doses are approved by the U.S. Food and Drug Administration (FDA) to treat patients with your type of constipation, and your doctor may prescribe it to you for your constipation even if you chose not to be in this study.

What will happen if I take part in this study?

If you decide to join this study, you will sign this form and then you will be asked to rate your pain and report to us when you have a bowel movement so we can see how long it takes after the medication is given to you, along with a pain score after your bowel movement.

Research Study Groups

To find out if one medication works better than another, this study has 3 groups. All three groups will receive a study drug that is known to have constipation-relieving effects. Each group will be given one of 3 medications. One group will have methylnaltrexone 12 mg administered subcutaneously (meaning right under the skin), another group will have methylnaltrexone 450 mg orally given as three 150mg tablets, and the last group will only receive one naloxegol 25mg oral tablet.

We will check your pain before you are given the medication, see how long it takes to have a bowel movement, and then check your pain after your bowel movement. We will also ask you about any negative effects you experienced. After the 60 minutes, your involvement in the study will be completed, and you will be treated by your Emergency Department team for any continuing pain or health concerns, if needed. If you leave the Emergency Department before a bowel movement and before 60 minutes, we will ask if we can call you to see what time you had a bowel movement.

Because we don't know which of the drugs is best, we will "randomize" you into one of the 3 study groups. "Randomize" means putting you into a group by chance. It is like flipping a coin or pulling a number from a hat. You will have a one in three chance of being placed in any group. A computer program chooses which group you go in. You and your care provider cannot choose which group you go into.

This study is "single blinded", which means that no one on the study team will not know which drug you received until the end of the study. This way, no one's expectations of what will happen in the study will affect the results. In an emergency, the study doctor can find out which drug you are getting.

Study Tests and Procedures

- If you take part in this study, you will have the following procedures:
- If you are a woman and could be pregnant, you will need a pregnancy test. You may have received a pregnancy test as part of your Emergency Department evaluation already, but if you haven't, a urine pregnancy test will be provided. We will tell you and your provider the result of this test.
- You will rate your pain before you get a test drug using a pain scale
- You will be given one of the 3 test drugs
- After 60 minutes you will be asked to rate your pain on the pain scale again if you have had a bowel movement. If a bowel movement takes longer than 60 minutes, we will ask that you rate your pain after the bowel movement happens.

We will keep the information we collect from you for this study to use in future research or to share with other investigators to use in future studies without asking for your consent again. Information that could identify you will be removed from your research data so no one will know that it belongs to you.

How Long Will I Be in the Study?

You will be in this study for about 60 minutes total, but it could be slightly longer if your bowel movement takes longer than 60 minutes.

Can I Stop Being In The Study?

You can stop being in the study at any time without giving a reason. If you stop being in the study, your regular medical care will not change. Leaving the study will not affect your future medical care at the University of Missouri.

There is no penalty to you if you do not join the study or if you leave it early. You will not lose any benefits you are entitled to if you leave the study.

If you decide to stop participating in the study, you should discuss your decision with the study doctor. The study doctor may decide to take you off this study at any time, even if you want to stay in the study. The study doctor will tell you the reason why you need to stop being in the study.

If necessary, the study doctor will arrange for you to continue your medical care with your regular doctor.

What Health Risks or Problems Can I Expect From The Study?

There are risks to taking part in any research study. There is a risk that you may get a drug dose that does not help your constipation. There may also be problems (also called side effects) we do not know about yet. If we learn about new important risks and side effects, we will tell you. We will tell you about any new information we learn that may affect your decision to continue taking part in the study.

Methylnaltrexone and naloxegol can affect people in different ways. Not everyone gets the same side effects. Side effects may be mild or very serious. Many go away soon after the drugs are stopped. Some side effects can last a long time or never go away. You may receive other drugs to make side effects less severe and uncomfortable. Complications of some of the side effects listed below may lead to life-threatening events such as *allergic reaction, diarrhea, gas, nausea, vomiting, muscle pain, headache, and stomach pain.*

We will closely watch everyone in the study for side effects. You need to tell the study doctor immediately if you have any problems, side effects, or changes in your health. Dr. Goddard's

telephone number is 573-884-4400. For more information about risks and side effects, ask the investigator or talk to your health care provider today.

- **Randomization risks**: You will be put into a group by chance. The drug you receive may turn out to be less effective or have more side effects than that in the other groups. It may also be less effective and have more side effects than other drugs available for constipation. While you are in this study, we will not know which drug you are getting. If your condition gets worse during the study and we need to know which drug you are getting, there will be a way for us to find out.

- **Reproductive Risks:** The effects of methylnaltrexone and naloxegol on a developing fetus are unknown but could cause harm. For this reason, it may be necessary to test for potential pregnancy if applicable. If you have any questions about the reproductive issues or about preventing pregnancy, please discuss them with the investigator or your doctor. You must tell the study doctor right away if you think you are pregnant.

Are There Benefits to Taking Part in the Study?

If you agree to take part in this study, there may or may not be direct medical benefit to you. You may expect to benefit from taking part in this research to the extent that you are contributing to medical knowledge. We hope the information learned from this study will benefit other patients with pain in the future.

There is no guarantee that taking part in this research will result in any improvement in your condition.

What Other Choices Do I Have?

You do not have to take part in this study. You are free to say yes or no. If you do not want to join this study, your doctor will discuss other choices with you. You may get drugs for constipation management including methylnaltrexone or naloxegol even if you do not take part in the study.

What About Privacy And Confidentiality?

The study team needs to access some of your health/personal information. This information comes from questions we ask you, forms you fill out, and your medical record. One risk of taking part in a research study is that more people will handle your personal health information. We are committed to respecting your privacy and to keeping your personal information confidential. The study team will make every effort to protect your information and keep it confidential to the extent allowed by law. However, it is possible that an unauthorized person will see it.

State and federal privacy laws (HIPAA) protect the use and release of your health information. If you decide to take part in this study, you also give us your permission to use your private health information, including the health information in your medical records and information that can identify you.

You have the right to refuse to give us your permission for us to use your health information. However, doing so would mean that you could not take part in this study.

The following identifiers will be obtained from your health records:

- ☒ Name
- ☒ Dates related to you
- ☐ Fax Number
- ☐ Social Security Number
- ☐ Health Plan Beneficiary Number
- ☐ Certificate or License Numbers
- ☐ Web Address (URL)
- ☐ Biometric Identifiers (finger/voice print)
- ☐ Any other characteristic that could identify you
- ☐ Address
- ☒ Telephone number(s)
- ☐ Email Address
- ☒ Medical Record Number
- ☐ Account Numbers
- ☐ Any vehicle or device serial number
- ☐ Internet Protocol (IP) Address(es)
- ☐ Photographic images

The following is the type of protected health information that will be used in the study:

- ☒ Radiology Images
- ☒ Radiology Reports
- ☐ EKG Recordings/Reports
- ☒ Progress Notes
- ☒ History and Physical Exams
- ☒ Operative Reports
- ☒ Pathology Reports
- ☒ Laboratory Reports
- ☐ Photographs/Video Recordings
- ☒ Discharge Summaries
- ☐ Health Care Billing or Financial Records
- ☒ Consultations
- ☒ Medications
- ☒ Emergency Medicine Reports
- ☐ Dental Records
- ☒ Demographics (age, race, etc.)
- ☒ Questionnaires, Surveys, Diaries
- ☐ Audio Recordings

☐ Social Security Number ☐ Other

We may share any of this information with the following:

- Authorized members and staff of the University of Missouri Institutional Review Board (IRB).
- Study monitors and auditors who make sure that the study is being done properly.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), and the Office for Human Research Protections (OHRP)

Any research information shared with outside entities will not contain your name, address, telephone or social security number, or any other personal identifier unless it is necessary for review or required by law.

The people who get your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it. Some of those people may be able to share your information with others without your separate permission.

Your permission for us to use and/or release your information will last until the end of the study unless you cancel your permission. You can cancel your permission at any time by writing to:

Investigator's Name: Kara B. Goddard
Institution: University of Missouri
Department: Emergency Medicine
Address: One Hospital Drive – DC029.1
Columbia, MO 65212

The information we have already collected may still be used for this research study, but we will not collect any more information after we receive your letter.

You have the right to access your protected health information that is obtained or created during this research project until the end of study ends.

If you have not already received a copy of the University of Missouri Healthcare Privacy Notice, you may request one. If you have any questions or concerns about your privacy rights, you may contact the Privacy Officer at 573-882-9054.

Information that does not become part of your medical record will be stored in the investigator's electronic/computer or paper files. Computer files are protected with a password and the computer is in a locked office that only study team members can open. Paper files are kept in a locked drawer in a locked office that only study team members can open.

Your records will be given a code number and will not contain your name or other information that could identify you. The code number that connects your name to your information will be kept in a separate, secure location. Information that may identify you may not be given to anyone who is not working on this study without your written consent, or if required by law.

The people who may use and/or release your research information include:

- Those working on the study team at the University of Missouri
- The members of the University of Missouri Institutional Review Board (IRB)
- Those who check on research activities to make sure it is being done correctly and safely
- The FDA
- Other government or inspection agencies

We may present the results of this study in public talks or written articles, but we will not use information that can identify you.

Can I See My Research Records?

If you join this study, you will be given one of 3 study drugs, without knowing exactly which one. This is called a "single blinded" study. This is a way of doing research when we want to compare drugs, and we don't want people's feelings about the drugs to affect the results.

If you ask to see your health records during this single blinded study, the study team cannot tell you which drug you got. This is because the study team is blinded to which drug you are getting. You would have to wait until all participants have completed the study. If we need the blinded information to treat you for an emergency, the study doctor will be able to find out.

Are There Any Costs To Being In The Study?

Some tests and procedures are only done because of the research. The study will pay for any medications or procedures that are only done because you are in this study. There is no cost to you for the study drug itself. However, you will be paying for the normal cost of your Emergency Department visit and your routine medical care. Any procedure related solely to research that would not otherwise be necessary will be explained. Some of these procedures

may result in added costs and some of these costs may not be covered by your insurance. Your doctor will discuss these with you.

In addition, the use of other medications to help control side effects could result in added costs that may or may not be covered by your medical insurance.

Will I be Paid for Taking Part in this Study?

There is no payment to you for taking part in this study.

What Happens If I Am Injured During The Study?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury. The University of Missouri, in fulfilling its public responsibility, has provided medical, professional and general liability insurance coverage for any injury in the event such injury is caused by the negligence of the University of Missouri, its faculty and staff.
The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while participating in the research projects of the University of Missouri.

In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number (573) 882-1181, at the Health Sciences Center, who can review the matter and provide further information.
This statement is not to be construed as an admission of liability.

What Are My Rights as a Study Participant?

Taking part in this study is voluntary. You do not have to take part. Your present or future medical care will not be affected if you decide not to take part.

If you do decide to take part, you can change your mind and drop out of the study at any time. This will not affect your current or future care at the University of Missouri Hospitals and Clinics. There is no penalty for leaving the study and you will not lose any benefits that you are entitled to receive.

If the study investigator decides to take you off the study, he/she will explain the reasons and help arrange for your continued care by your own doctor, if needed.

We will tell you about any new information discovered during this study that might affect your health, welfare, or change your mind about taking part.

Where Can I Get More Information About This Study?

A description of this clinical trial will be available on 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.

Who Can Answer My Questions About The Study?

If you have more questions about this study at any time, you can call Dr. Goddard at 573-884-4400. You may also contact the University of Missouri Institutional Review Board (IRB) if you:

- Have any questions about your rights as a study participant;
- Want to report any problems or complaints; or
- Feel under any pressure to take part or stay in this study.

The IRB is a group of people who review research studies to make sure the rights of participants are protected. Their phone number is 573- 882-3181.

If you want to talk privately about your rights or any issues related to your participation in this study, you can contact University of Missouri Research Participant Advocacy by calling 888-280-5002 (a free call), or emailing MUResearchRPA@missouri.edu.

We will give you a copy of this consent form. Please keep it where you can find it easily. It will help you to remember what we discussed today.

Signature of Study Participant for Consent to Participate in Research

By signing my name below, I confirm the following:

- I have read/had read to me this entire consent form.
- All of my questions were answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits were explained to me.
- I voluntarily agree to take part in this research study. I have been told that I can stop at any time.

Subject's Signature	**Date**

Signature of Witness (if applicable)*	**Date**

**A witness is required when a participant is competent to provide consent but is blind, or cannot read or write.*

Signature of Person Authorized to Obtain Consent*

I have explained the purpose of the research, the study procedures (identifying those that are investigational), the possible risks and discomforts and potential benefits of the study, and have answered questions regarding the study to the best of my ability.

Signature of Person Authorized to Obtain Consent	**Date**

**This signature is required for FDA regulated research and/or research that involves any medical procedure or surgical treatment*