Reduce Crohn's-Associated Diarrhea With Sodium Channel Therapy
NCT04456517
October 14, 2020

VUMC Institutional Review Board
Informed Consent Document for Research

Study Title:	REACT Trial: A randomized, double blind, placebo-controlled, crossover study of ranolazine for the treatment of Crohn's Disease-associated diarrhea
Version Date:	2020.10.08
PI:	Dawn Beaulieu, MD

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
The purpose of this study is to test the safety and effectiveness of the drug ranolazine in reducing Crohn's disease-associated diarrhea. Ranolazine is approved by the US Food & Drug Administration (FDA) for chronic angina (a heart condition). All participants in this study will take ranolazine for 12 weeks and placebo (pills that do not contain the drug) for 12 weeks, which means that participants will be enrolled in the study for a total of 24 weeks. During the 24 weeks, you will come to the Vanderbilt IBD Center for three study visits that will each last about 90 minutes. At these visits you will answer questions about your Crohn's symptoms. You will also receive a text message every day during the 24 weeks prompting you to report daily number of loose stools, any use of antidiarrheal medication, and your study medication doses. All participants are allowed to continue taking all of their standard medications during the study. There is no cost to you for taking part in this study.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have Crohn's disease and are experiencing frequent diarrhea. The purpose of this study is to compare the safety and effectiveness of the drug ranolazine to the safety and effectiveness of placebo (pills that do not contain the drug) in reducing Crohn's disease-associated diarrhea and other symptoms. Ranolazine is approved by the US Food & Drug Administration (FDA) for chronic angina (a heart condition), but ranolazine is considered investigational for the purposes of this study and some participants may experience side effects. All participants in this study will take ranolazine for 12 weeks and placebo for 12 weeks, which means that

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participants will be enrolled in the study for a total of 24 weeks. During the 24 weeks, you will come to the Vanderbilt IBD Center for three study visits. At these visits you will answer questions about your Crohn's symptoms. When all study activities are complete, we will review the results of our testing to see if there are similarities among the patients who improved with ranolazine treatment. Approximately 50 people will be evaluated at Vanderbilt University Medical Center to determine if they are eligible to take part in this study. We expect that approximately half of the people we screen will be eligible to enter the treatment study. Our goal is to have 20 participants complete the full study: 10 patients with active Crohn's and 10 patients in remission.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
Side effects association with the use of ranolazine: Ranolazine's safety profile has been established by extensive clinical experience. Some drugs are known to interact with ranolazine and may cause adverse events. For your safety, you must tell the study doctor or nurse about all the drugs you are taking, including over-the-counter drugs and herbals, before you start the study and before taking any new drugs while you are on the study. When used properly and not at the same time as other drugs that are known to interact with ranolazine, ranolazine has been shown to be safe and well-tolerated. The most common side effects include dizziness, nausea, constipation, headache, and asthenia (weakness or lack of energy). Other studies have found that less than 2% of patients experience these side effects and therefore, these side effects are uncommon.

Ranolazine pregnancy risks: Ranolazine treatment may hurt an unborn child. If you become pregnant while you are in this study, you must tell your doctor at once. Also, women must not breastfeed while in this study. If you are a woman and are able to become pregnant, you will have a urine test to make sure that you are not pregnant before you receive treatment in this study.

Risks that are not known:
Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

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Good effects that might result from this study:
The benefits to science and humankind that might result from this study: A possible benefit to science and humankind is that we may learn about using ranolazine as a new treatment for Crohn's disease-associated diarrhea. However, there is no guarantee that participants will benefit from being in this research study.

Procedures to be followed:
This is a randomized, double-blind, placebo-controlled, crossover study, which means that if you agree to be in this study, you will take pills containing the study drug, ranolazine, and placebo pills that look like the study drug but do not contain any drug. Crossover means that you will take one of these treatments first and then the other second. Randomized means that it is up to chance (like flipping a coin) which order you will take ranolazine and placebo. Double-blind means that you, the study doctor, and the study team will not know which order you will take ranolazine and placebo.

You will take 1 study pill twice a day.

If you agree to be in this study your involvement will last about 24 weeks (6 months). Below you will find information on each of the five study visits and what you can expect if you agree to take part in this study.

In-person Visit 1: This visit will last about 1.5 hours. The following will occur at this visit.

- The study team will discuss the study with you and answer all of your questions.
- The study team will discuss your medical history with you.
- If you are a woman who could be pregnant, a urine pregnancy test will be collected to make sure you are not pregnant. The study team will also discuss birth control options with you.
- You will complete symptom and quality of life questionnaires.
- You will be placed into either the ranolazine first/placebo second or placebo first/ranolazine second group.
- You will receive the first study medication to take home with you.
- The study team will discuss mobile phone data collection with you.

Mobile phone data collection (daily): You will receive a text message every day prompting you to report daily number of loose stools, any use of antidiarrheal medication, and your study medication doses.

In-person Visit 2 (12 weeks after in-person Visit 1): This visit will last about 1.5 hours. The following will occur at this visit.

- The study team will discuss how you are feeling.

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- The study team will review mobile phone data collection with you.
- You will return the empty bottles you were given with your study drug.
- You will get a new supply of study drug to last you until your next visit (this is when you switch to the second medication).
- If you are a woman who could be pregnant, a urine pregnancy test will be collected to make sure you are not pregnant. The study team will also discuss birth control options with you.
- You will complete symptom and quality of life questionnaires.

Mobile phone data collection (daily): You will receive a text message every day prompting you to report daily number of loose stools, any use of antidiarrheal medication, and your study medication doses.

In-person Visit 3 (12 weeks after in-person Visit 2): This visit will last about 1.5 hours. The following will occur at this visit.

- The study team will discuss how you are feeling.
- The study team will review mobile phone data collection with you.
- You will return the empty bottles you were given with your study drug.
- You will complete symptom and quality of life questionnaires.

Payments for your time spent taking part in this study or expenses:
If you are eligible and choose to participate, you will receive a $150 compensation upon study completion ($50 for each of the three study visits). You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your SSN for this purpose. You will also need to provide your address so that a check can be mailed to you. Your SSN is obtained for payment purposes only and it will not be retained for research purposes. It may take up to 4-6 weeks to receive your check following completion or withdrawal from the study.

Costs to you if you take part in this study:
There is no cost to you for taking part in this study.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

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There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Dawn Beaulieu at (615) 936-6956 or Erin Landry at (615) 322-4573. If you cannot reach the research staff, please contact the Director of Clinical Research at (615) 422-4643.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
You will be withdrawn from the study if the study doctors decide it is best for you. If the study doctors withdraw you from the study, you will be told the reason.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:
Data will be maintained in paper and computer files that will be locked and password-protected. Only the study team will have access to identifying information. Information will be maintained indefinitely by the Principal Investigator.
This study has support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

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It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
You will have the opportunity to receive results that emerge from the study. Some results will be available during the study and some will be available at the conclusion of the study after the results are analyzed. Please know that the delay in receiving results may be long.

Screening results: You will receive the results of the screening tests even if you are not eligible to join the study. The screening tests include a urine pregnancy test. You will be told your results as soon as they are available. You may talk with the study staff about the meaning of your results and if you have further questions.

Individual and overall study results: When the results of the study are available to share, we will inform you of the overall summary results of the study. We will also share your individual results with you upon request. Results will be available within 12 months after the conclusion of the overall study via letter, phone call, or visit in our office. Your individual results will include which study group you were in (ranolazine-first or placebo-first group) and may include the measurements we took from you (survey results, mobile phone data collection results) and, if appropriate, how they compare with other participants in the study.

Exploratory results: In the course of research, we may generate results that could be of medical significance or personal use to you. In those cases, we reserve the right to contact you and provide the option of receiving those results. If you do not hear from us, this does not mean you should not continue with regular medical care.

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The researchers do not plan to contact your regular doctors with any study results. If you have any questions, you should contact Dr. Dawn Beaulieu at (615) 936-6956.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this

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consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
Time	Printed Name and Title