Roflumilast or Azithromycin to Prevent COPD Exacerbations (RELIANCE) Trial

NCT Number: NCT04069312

Participating Site (pSite) Informed Consent Form

23 June 2023

STUDY2022-1258-CR003
Effective: 1/9/2025
Expires: 1/8/2026
UIC Office for the Protection of Research Subjects

RESEARCH PARTICIPANT

INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title:	RofLumilast or Azithromycin to preveNt COPD Exacerbations (RELIANCE)
Sponsor:	University of Illinois at Chicago
Funder:	Patient-Centered Outcomes Research Institute (PCORI)
Network Principal Investigator:	Jerry A. Krishnan, MD, PhD
Department:	Department of Medicine Division of Pulmonary, Critical Care, Sleep, and Allergy University of Illinois at Chicago 1220 S. Wood St., M/C 619, Chicago, IL 60608

Site Principal Investigator Name and Title:	Daniel Ouellette, MD
Department:	Pulmonary
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Additional contact information:

Participant name:

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What should I know about this study?

You are being asked to join a research study. A member of the research team will explain the study and how it works. They will also explain how the study will affect you.

Joining the study is your choice. You do not have to join this study. Your doctors, this hospital, and other medical centers will continue to care for you whether you join the study or not. If you choose to join this study and you have had your questions answered, you will be asked to sign this form. When you are done, you will get a copy of the signed consent form.

This consent form explains the study and your part in it. This includes:

- all the study steps
- the risks and benefits of joining the study
- steps to protect your data and privacy

Please read this consent form carefully. Take as much time as you need. Ask your doctor or someone on the research team to explain any words or ideas you don't understand. They are here to help you make this decision. You may also want to talk to your family or friends about this study.

Why is this study being done?

RELIANCE is a study comparing two drugs that doctors are planning to prescribe for their patients. You are eligible for this study because your doctor was planning to prescribe either Azithromycin or Roflumilast to help control your lung disease and you and your doctor do not have a preference for either medicine. We are trying to learn which works better for people with Chronic Obstructive Pulmonary Disease (COPD). COPD is a lung disease.

Today, doctors use both Roflumilast and Azithromycin to treat COPD. Research shows that people who take Roflumilast or Azithromycin go to the hospital less often for COPD attacks. Roflumilast has been approved by the Food and Drug Administration (FDA) as a treatment for COPD with chronic bronchitis. Azithromycin has *not* been approved by the FDA for treating COPD. But Azithromycin has been approved by the FDA for treating infections. Doctors are allowed to use Azithromycin to treat other medical problems when they think it will help their patients.

RELIANCE will test if Azithromycin is as good as Roflumilast at preventing COPD attacks and hospital visits. It will also look at side effects of each drug to see which is better tolerated by people with COPD. Today, doctors don't know which drug works best for which patients. There are different types of people with COPD, such as current smokers and past smokers. We want to know if one of these drugs works better for people who currently smoke.

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How many people will take part in the study?

We expect 1,250 people to join this study. You have been asked to join this study because you were in the hospital recently for COPD and you already take medicine for COPD. RELIANCE has research sites across the country. This will allow many different types of people to join the study.

How long will I be in the study?

You could be in the study for up to 36 months (3 years). This depends on when you join. People who join at the beginning of the study will be in the study for 3 years. People who join later in the study will be in the study for a shorter time. Everyone who joins will be in the study for at least 6 months.

What happens when I join the study?

There is only one clinical visit for this study. This visit may be in-person or by phone. During or just after this visit, you will sign the consent. After you have signed the consent, you will talk with a study doctor and coordinator. They will ask you questions, and your study doctor will decide if you meet the conditions to join the study.

Once you both agree you should join the study, you will be randomized to take either Roflumilast or Azithromycin. Randomization is like flipping a coin. Neither you nor your doctor(s) choose the study drug. You have an equal chance of getting Roflumilast or Azithromycin.

How you take the medicine is up to you and your doctor. Being in the study does not change how much or how long you take the study drug. The goal of the study is to carefully track what happens to people who are prescribed either of these drugs.

Your doctor will decide what dose of the study drug you should take. Your doctor can also decide to change the dose or stop the study drug. Your doctor may choose to do this based on your body's reaction to the study drug or whether the study drug is helping you.

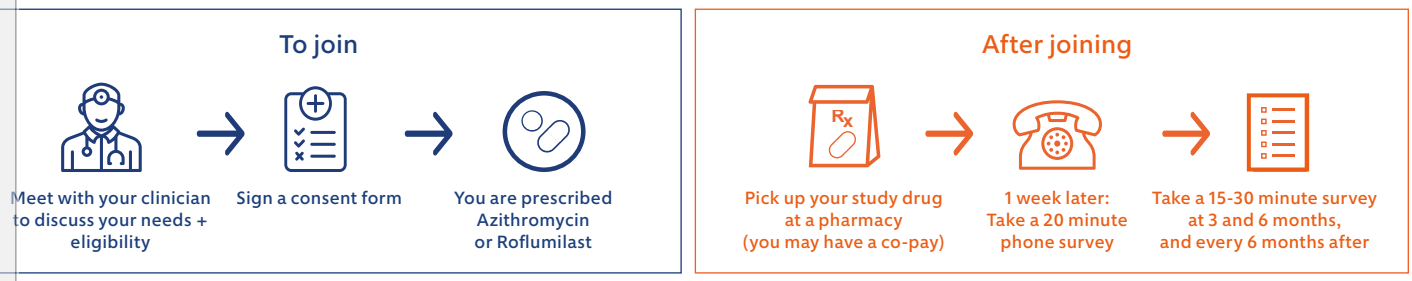
Your doctor will give you a prescription for either Roflumilast or Azithromycin. You should fill the prescription at your pharmacy, just like any other prescription.

If the study doctor is not your usual doctor, we will inform your usual doctor that you've joined the study and tell them the study drug and dose you are receiving.

You can choose how to answer your study questions. You can have us call you and answer study questions by phone. Or you can use the RELIANCE patient website and enter your answers yourself. The study team member at your clinic can help you register and create an account. Once you have an account, you can use it to answer your study questions. Answering study questions online will take about 15-20 minutes each time.

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AT-A-GLANCE: What to expect if you join RELIANCE



Enrollment	**Agree to join the study and sign the consent form.** • You agree to join the study. You sign the consent form. • You will answer questions about yourself to allow the study doctor to make sure you are eligible for the study. This will include your current illnesses, hospital stays, medicines, and smoking history. • You give us information about you. This will include information about your health and wellbeing, your name, address, telephone number, email, sex, race, medical record number, social security number (or health insurance claims number or taxpayer ID), and health insurance provider. If you are enrolled in Medicare, we will also ask for your enrollment number. • Get a prescription for the study medicine you are assigned. *This should take about 30 minutes. Your clinic appointment with your doctor may take longer.*
Week 1	**Have a check-in call with our call center.** • They will ask if you filled your prescription. They will also ask if you have started taking the study drug, and about your health and wellbeing. *This should take about 20 minutes.*
At month 3, at month 6, and then every 6 months	**Have a follow-up call with our call center.** • They will ask about your health and wellbeing. They will also ask if you are still taking Roflumilast or Azithromycin, and the healthcare you have received since your last call. You can also choose to use the RELIANCE patient website to answer these questions. *This should take 20 minutes.*
End of the study	**Have a final call with our call center.** • If you go back to the hospital, the study team will call you one last time to ask you questions about your hospital stay and medicines you were given. They may also ask you questions about your experience in the study. *This should take 10 to 15 minutes.*

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What happens when I join the study? *cont'd*

We can remind you to answer your study questions. We will send reminder emails or text you that it's time to answer study questions. If you don't log into your account, we will call you to take your answers over the phone. All of our calls for the study are recorded for quality and training purposes. The recordings are kept for up to three years after the study results have been finalized, and will then be deleted.

We will ask your permission to collect information about your health. We would like permission to see your medical records and insurance records. This will help us see if you have been in the hospital, the emergency room, or an urgent care center. We would also like to review your pharmacy records to see if the prescription for the study drug has been filled. If you are enrolled in Medicare, we will work with the Food and Drug Administration (FDA) Sentinel Initiative to review the Centers for Medicare and Medicaid Services (CMS) records about your healthcare. This will help us get more complete information about your health when taking the study drug. Lastly, we will review records that the Centers for Disease Control (CDC) keeps about deaths. Without the information above, we will not be able to tell if the medicines are helping or not. By agreeing to participate, you are giving your permission to collect this information about you.

What are the risks and discomforts of the study?

Your COPD might not improve from being in this study. Uncontrolled COPD can be life-threatening. This study does not replace clinical care for your COPD. Therefore, it is important that you follow your usual care for COPD. That means see your usual doctor for treatment and get emergency treatment if needed.

Roflumilast and Azithromycin may have side effects. If you have a bad reaction to Roflumilast or Azithromycin you should contact your usual doctor. If the reaction is serious or life threatening get medical attention right away.

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Study drug risks
Roflumilast

In studies of 4,438 people taking Roflumilast and 4,192 people taking placebo (a pill that contains no active drug), some people reported side effects. The most common side effects (>2%) in people taking Roflumilast or placebo were diarrhea, weight loss, nausea, headache, back pain, influenza, insomnia, dizziness, and decreased appetite.

Roflumilast may cause mental health problems including suicidal thoughts or behavior. Some people taking Roflumilast may develop mood or behavior problems. Your doctor will be able to talk with you about this, and whether or not they think it may affect you.

	People taking Roflumilast	**People taking placebo**
diarrhea	**9.9** of every 100 people	**2.7** of every 100 people
weight loss	**7.5** of every 100 people	**2.1** of every 100 people
nausea	**4.7** of every 100 people	**1.4** of every 100 people
headache	**4.4** of every 100 people	**2.1** of every 100 people
back pain	**3.2** of every 100 people	**2.2** of every 100 people
influenza	**2.8** of every 100 people	**2.7** of every 100 people
insomnia	**2.4** of every 100 people	**1** of every 100 people
dizziness	**2.1** of every 100 people	**1.1** of every 100 people
decreased appetite	**2.1** of every 100 people	**.4** of every 100 people
anxiety	**1.4** of every 100 people	**.9** of every 100 people
depression	**1.2** of every 100 people	**.9** of every 100 people
suicidal thoughts	**.07** of every 100 people	**.02** of every 100 people

Your study doctor can explain why some people who take a placebo still report side effects.

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Study drug risks

Azithromycin

In the MACRO study, 558 people were prescribed Azithromycin every day and 559 people were prescribed placebo every day for 1 year. Some people reported side effects. Common side effects in people taking Azithromycin or placebo were decreased ability of antibiotics to fight infections, hearing loss, ringing in the ears, pneumonia, gastrointestinal issues, and abnormal heartbeat. Sometimes these side effects changed depending on how long

	People taking Azithromycin	People taking placebo
decreased ability of antibiotics, like Azithromycin, to fight infections	**81** of every 100 people	**41** of every 100 people
hearing loss	**25** of every 100 people	**20** of every 100 people
pneumonia	**5** of every 100 people	**7** of every 100 people
nausea, vomiting, abdominal pain or diarrhea	**3** of every 100 people	**4** of every 100 people
ringing in the ears	**1** of every 100 people	**1** of every 100 people
abnormal heartbeat	fewer than **1** of every 100 people	fewer than **1** of every 100 people

Your study doctor can explain why some people who take a placebo still report side effects.

What are other risks?

You may get tired or bored of answering the study questions. Some people can feel uncomfortable or get worried when answering some study questions. You do not have to answer any question that you do not want to answer.

You may get tired of study reminders. You can ask us to stop sending you reminders. You can also ask us to stop calling you. You can choose how we remind you. For example, you can ask that we text you rather than call you.

Your health information may become known to people who are not authorized to see it.

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Are there risks related to pregnancy?

Women who think they might be pregnant may not join RELIANCE. If you think you might be pregnant, ask your doctor for a pregnancy test before you agree to join the study. There are risks to the fetus or embryo related to exposure to these drugs.

What if there is new information that changes my mind about joining?

We may learn important new information during the study. We will share this with you. This new information could include new risks to people who are taking study drugs. Or it could include new benefits for people taking the study drugs. Or we might learn there are new treatment options that might cause you to change your mind about staying in the study. If we share new information with you, we may need to have you sign a new consent form to stay in the study.

What are the benefits of joining the study?

You may or may not benefit from taking Roflumilast or Azithromycin. Both drugs may help people who are at a high risk for going into the hospital for COPD. There may also be no benefit to you in joining this study.

Your participation in RELIANCE may help others with COPD in the future.

What other options are there?

You have the option to not join this study and still receive a prescription for Azithromycin or Roflumilast for your COPD.

What are the costs of joining RELIANCE?

There are no costs for joining the study. You or your insurance will be responsible for paying for your prescription. Roflumilast may cost more than Azithromycin.

This study does not require any procedures, tests, or devices.

Will I be paid for joining RELIANCE?

You will receive a $100 gift card when you join in the study. You will receive a $25 gift card for each time you answer your study questions (every 3-6 months). You can answer study questions online or by phone.

If you do not finish the study, you will be paid for the study questions you have finished. The total amount of money you receive will depend on when you joined the study and how many sets of study questions you answer. The longer you are in the study, the more sets of study questions you can be paid for.

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Will I be paid for joining RELIANCE? *cont'd*

You will receive your payment in the mail within two weeks of when you complete your study questions or by email, depending on your preference.

We may need to collect your social security number or Taxpayer Identification Number. This will allow us to send you your payment. We might also need it for tax reports to the United States Internal Revenue Service.

Can I leave the study? Or be taken out of the study?

You have the right to leave the study at any time. If you leave the study early, you will continue to receive care from your doctor. For your safety, however, you should talk to your study doctor about how to best leave the study. The study doctor may suggest you see your doctor to make sure it is safe to stop taking the study drug. The study doctor may also ask you to answer the final study questions before leaving the study.

The research team and study funder have the right to take you out of the study. They may do this without your consent. Reasons to take you out of the study include:

- The study doctor decides that staying in the study would be harmful to you.
- You become pregnant.
- The study is stopped.

You will still be paid If you leave the study or are asked to leave the study. You will be paid as described above.

Your Authorization for release of health information for this research study does not have an expiration date, but can be canceled sooner if you decide to withdraw your permission. You may change your mind and cancel the Authorization for release of your health information at any time.

To cancel this Authorization, you must write to:

Dr. Daniel Ouellette
Henry Ford Health System
2799 W. Grand Blvd.
K-17
Detroit, MI 48202

If you cancel this Authorization, you may no longer be allowed to take part in the research study. Even if you cancel this Authorization, the researchers may still use and disclose health information they have already obtained as necessary to maintain the integrity and reliability of the research and to report any adverse (bad) effects that may have happened to you.

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What if I am injured from participating in the study?

You may experience side effects or injury from taking the study drugs. If you believe that taking part in this study has made you sick or injured, you can get medical care at:

- Henry Ford Health System (HFHS) OR
- Your usual care doctor OR
- The treatment center or clinic of your choice.

If you get medical care, please take a copy of this document with you. It may help the doctors at the treatment center give you the care you need. It will also help the doctors contact your study doctor, if they need to.

You can also contact your study doctor to talk about your illness or injury. See page 1 for the name and phone number of your study doctor.

If you have an urgent medical problem from taking part in this study, call 911 and seek care.

You or your insurance company will be billed for this medical care. Your insurance company may not pay for some or all of this medical care because you are participating in a research study. There are no plans for HFHS to provide free medical care. There are no plans for HFHS to pay for research-related illnesses or injuries. There are no plans for HFHS to give other forms of compensation (such as lost wages or pain and suffering) for research related illnesses or injuries. There is no federal, state, or other program that will compensate you or pay for your medical care if you are injured as a result of participating in this study.

By signing this form you will not give up any legal rights.

Who can answer my questions about the study?

The research team is here to answer your questions. You have talked to members of the research team and had the chance to ask questions. You can ask them questions about any and all parts of the study.

You can contact the study leader, Dr. Jerry Krishnan, if you have more questions about the study. You can call him at 1 (833) OUR-COPD (1-833-687-2673). You can email him at reliance@uic.edu. Contact him if:

- You have any questions about this study or your part in it,
- You feel you have had a research-related injury (or a bad reaction to the study drug),
- You have questions, concerns or complaints about the study.

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Who can answer my questions about the study? *cont'd*

You can call the Office for the Protection of Research Subjects (OPRS) if you have questions about your rights as a study participant. You can also call them if you have concerns, complaints, or feedback on the study. You can call them at (312) 996-1711 or toll-free at (866) 789-6215. You can also email them at uicirb@uic.edu.

Are there any conflicts of interest?

Dr. Ouellette is one of the researchers conducting this study. Dr. Ouellette may also be the doctor you see for clinical care. As your doctor, Dr. Ouellette's first responsibility is to provide you the best care possible. Dr. Ouellette is also interested in improving care for his patients and has agreed to enroll patients who are eligible and want to be in the study. So in addition to providing you medical care he is also part of the research team and receive some funding from the study.

This institution also receives a stipend for each person enrolled in the study. The payment is to cover time and effort of Dr. Ouellette and other staff to carry out the research.

Before entering this study or at any time during the research, you may ask for a second opinion about your care from a clinician who is not associated with this project. You are not obligated to participate in any research project offered by your clinician.

What about privacy and confidentiality?

The people who will know that you are a research subject are members of the research team, and if appropriate, your physicians and nurses. No information about you, or provided by you, during the research, will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are injured and need emergency care or when the UIC Office for the Protection of Research Subjects monitors the research or consent process) or if required by law.

By signing this consent form, you agree that we may collect, use and release your personal and health information for the purpose of this research study. We may collect and use:

- Your existing medical records.
- New health information created during this study.
- Health insurance and other billing information.

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What about privacy and confidentiality? *cont'd*

During the conduct of the research, the researchers may use or share your health information with:

- Each other and with other researchers involved with the study
- Sponsor of the study, Patient Centered Outcome Research Institute
- Henry Ford Health System and representatives of this institution (The Principal Investigator and his/her associates who work on, or oversee the research activities)
- Members of the Data Coordinating Center at Johns Hopkins University
- Members of the Call Center at the University of Illinois at Chicago
- Government Regulatory Agencies, such as the Food and Drug Administration (FDA) and the Office for Human Research Protections (OHRP)
- Researchers at Harvard Pilgrim Health Care Institute and Duke University involved in analyzing the data
- Chicago Area Institutional Review Board (CHAIRb)
- UIC Office for the Protection of Research Subjects
- State of Illinois Auditors
- Your insurance company or others responsible for paying your medical bills
- Other researchers at other institutions participating in the research

Once your information has been released according to this consent form, it could be released again and may no longer be protected by federal privacy regulations.

This consent form, test results, medical reports and other information about you from this study may be placed into your medical record. Generally, you are allowed to look at your medical record.

A possible risk of the research is that your participation in the research or information about you and your health might become known to individuals outside the research. The study team uses methods to protect your data including encryption (converting your data to a code to help prevent unauthorized access), limiting the number of people who have access to your data, using strong password protection, and using secure servers.

Information from this study could be published in journals or presented at meetings by HFHS or others. If either of these happens, your name, identifying pictures, other direct identifiers, and other personal information will not be used in any public presentation or publication about this study unless you sign a separate consent allowing that use.

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What about privacy and confidentiality? *cont'd*

Other researchers who are not involved in RELIANCE may ask to see your study data after the study is completed. Before we send them study data, we remove names, birth dates, social security numbers, and other information that could be used to identify you. This makes it very hard for anyone to know who you are. These researchers include other researchers in the PCORI network. It may also include qualified researchers outside the network.

We follow rules to protect your information. These rules include both federal and state laws, such as the HIPAA (Health Insurance Portability and Accountability Act) Privacy Rule. When you sign this form, you give us permission to use and share your health information now protected by the Privacy Rule. Your permission is called "authorization".

When your health information is given to people outside of the research study, those agencies that receive your health information may not be required by federal privacy laws (such as the Privacy Rule) to protect it. They may also share your information with others without your permission, if permitted by laws that they have to follow.

We cannot enroll you in this study unless you allow us to use and share your information. You do not have to give us this permission. But if you do not give us permission, you cannot join the study. You do not have to sign this consent to release your medical information and may cancel it at any time.

If you decide not to sign this consent or cancel your consent, you cannot participate in this study. If you notify us that you wish to stop participating in this study, we may continue to use and release the information that has already been collected. To cancel your consent, send a written and dated notice to the principal investigator at the address listed on the first page of this form.

This consent to use and release your personal and health information will not expire at the end of this research study. When you sign this form, you give us permission to use and share your information as we have described without a time limit.

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

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What are my rights as a participant?

Taking part in this study is your choice. If you choose not to participate in this study, your care at your study site will not be affected. You may choose to leave the study at any time. Leaving the study will not affect your care at your study site. See page 1 for the name of your study site.

Signing this form indicates that you agree to join the study. Signing this form also indicates that you give permission to the research team to use and share your health information for the study. You do not give up any of your legal rights by signing this consent form.

You will be given a signed copy of this consent form. If you have not already received a copy of the Notice of Privacy Practices, you should ask for one.

We will give you a copy of this signed and dated form

I agree to be contacted by the RELIANCE research team about joining future studies.

This is optional and not required to join the RELIANCE study.

☐ I agree ☐ I do not agree

PARTICIPANT SIGNATURE	PRINTED NAME	DATE

For the person obtaining consent: I attest that all the elements of informed consent described in this document have been discussed fully in non-technical terms with the subject [or the subject's legally authorized representative]. I further attest that all questions asked by the subject [or the subject's legal representative] were answered to the best of my knowledge.

SIGNATURE OF PERSON OBTAINING CONSENT	PRINTED NAME	DATE