

Online Supplement

Original Research

Rationale and Design of the Roflumilast or Azithromycin to Prevent COPD Exacerbations Clinical Trial

Jerry A. Krishnan, MD, PhD¹ Janet T. Holbrook, PhD² Elizabeth A. Sugar, PhD² Richard Albert, MD³ Steve Rennard, MD⁴ Nina Bracken, APRN¹ Jiaxian He, MS² Marie Bradley, PhD, MSc PH, MPharm⁵ Kevin Coughlin, MA⁶ Candace C. Fuller, PhD, MPH⁶ Bradley Hammill, DrPH, MA⁷ Elisha Malanga⁸ Vincent M. Malanga⁸ David Mannino, MD, MPH⁸ Richard A. Mularski, MD, MCR, MSHS⁹ Hugh Musick, MBA¹ Jean Rommes, PhD⁸ Julie DeLisa, MA¹ Sengwee Toh, ScD⁶ Robert A. Wise, MD²

¹University of Illinois Chicago, Chicago, Illinois, United States

²Johns Hopkins University, Baltimore, Maryland, United States

³University of Colorado Anschutz, Aurora, Colorado, United States

⁴University of Nebraska Medical Center, Omaha, Nebraska, United States

⁵U.S. Food and Drug Administration, Silver Spring, Maryland, United States

⁶Harvard Pilgrim Health Care Institute, Boston, Massachusetts, United States

⁷Duke University, Durham, North Carolina, United States

⁸COPD Foundation, Miami, Florida, United States

⁹Kaiser Permanente Northwest, Washington, D.C., United States

Supplement Table 1. RELIANCE Clinical Centers and physicians using the Community Partner Referral Pathway

Clinical Centers (n=26)	Community Partners (n=41) nominated by Clinical Centers or members of the Executive Committee
1. Baystate Health PI: O’Neil Green, Co-I: Nicole Strieter	1. Anil Ghimire (Chronic Lung Disease Clinic - Family Health Care Network)
2. Baylor Scott & White Health – North PI: Mark Millard, Co-I Jeffrey Kopita	
3. Cleveland Clinic PI: Umur Hatipoglu	2. Randall Harris (Akron General Hospital) 3. Vickram Tejwani (Hilcrest Hospital) 4. Ian Oppenheim (Medstar Georgetown University Hospital) 5. Abhishek Bhardwaj (Coast Pulmonary & Internal Medicine Associates)
4. Duke University PI: Christopher Mosher, Co-I: Loretta Que	
5. Henry Ford Health System PI: Daniel Ouellette, Co-I: Jovica Veljanovski	6. Kevin Almerico (Miami Pulmonary Specialists)
6. Houston Methodist PI: Rodney Folz	
7. Johns Hopkins University PI: Niru Putcha, Co-I: Robert Wise	7. Michael Lester (Vanderbilt University) 8. Blake LeMaster (Vanderbilt University) 9. Adrienne Conger (Vanderbilt University) 10. Mollie Anderson (Vanderbilt University) 11. Sara Carson (Kootenai Health)
8. Kaiser Permanente Northwest PI: Richard Mularski, Co-I: Britta Torgimson-Ojerio	12. Ben Moss (Hillsboro Medical Center)
9. Mount Sinai Health System PI: Linda Rogers	13. Wanda Choy (The Valley Hospital) 14. Alexandra Adams (UR Thompson Health Pulmonary Clinic) 15. Alissa Greenberg Lee (Connecticut Northeast Medical Pulmonary Group) 16. Dan Howell (Woodhull Hospital Brooklyn, NY)
10. NorthShore University HealthSystem PI: Shashi Bellam, Co-I: Stacy Raviv	
11. Northwell Health PI: Bushra Mina, Co-Is: Jessica Homan, Oki Ishikawa, Jennifer	
12. Northwestern University PI: Ravi Kalhan, Co-I: Sharon Rosenberg	17. Alexis Wolfe (Northwestern Lake Forest Hospital)
13. Ochsner Health New Orleans PI: Susan Gunn, Co-I: Leonardo Seoane	
14. Ohio State University PI: Phillip Diaz, Co-I: Sonal Pannu	
15. Temple University	


PI: Gerard Criner, Co-I: Nathaniel Marchetti	
16. University Hospitals Cleveland Medical Center PI: Catalina Teba	
17. University of Alabama at Birmingham PI: Surya Bhatt, Co-I: Mark T. Dransfield	
18. University of California Davis PI: Mark Avdalovic, Co-I: Brooks Kuhn	18. Brett Schaeffer (Erlanger Health System)
19. University of Illinois Chicago PI: Jerry Krishnan, Co-Is: Christie Brillante, Min Joo	19. Rodrigo Vazquez Guillamet (Washington University St. Louis) 20. Jennifer Minoff (Hannibal Regional Healthcare System) 21. Mehdi Mirsaeidi (University of Florida Health-Jacksonville)
20. University of Iowa PI: Alejandro Comellas, Co-I: Spyridon Fortis	22. Iliya Amaza (UW Health Pulmonary Clinic)
21. University of Kansas PI: Mario Castro, Co-I: Chase Hall	23. James Krings (Washington University St. Louis) 24. Dan Reynolds (Washington University St. Louis) 25. Zachary Lonjers (Washington University St. Louis)
22. University of Michigan PI: MeiLan Han, Co-I: Wassim Labaki	
23. University of Missouri – Truman Medical Center PI: Gary Salzman	26. Amine Bourbia (Harbin Clinic) 27. Gabe Anders (Bothwell Regional Health Center)
24. University of North Carolina PI: Brad Drummond	28. Jill Ohar (Wake Forest Baptist)
25. University of Pittsburgh Medical Center PI: Frank Sciurba, Co-I: Corrine Kliment	
26. University of Vermont PI: Anne Dixon, Co-I: David Kaminsky	29. Veronika Jedlovszky (Rutland Regional Medical Center, Vermont) 30. Brittany Duchene (Northeastern Vermont Regional Hospital) 31. Ram Baalachandran (Central Vermont Medical Center) 32. Suman Majumdar (Central Vermont Medical Center) 33. Facundo Stingo (Rutland Regional Medical Center)
Nominations by members of the RELIANCE Executive Committee	34. Jeannette Zinggeler Berg (Kootenai Clinic Lung & Asthma) 35. Scott Meehan (Multicare Health System) 36. Sankaran Krishnan (Boston Children's Health Physicians) 37. Catherine Hooper Miele (Virginia Mason) 38. Timothy Spooner (Centra Health) 39. Kaleb Veit (University of Nebraska) 40. Tamer Hudali (The Lung and Sleep Center of North Texas) 41. Wilfor Diaz Fernandez (Beth Israel Deaconess MC Milton)

Footer for Supplement: Clinical Centers and their Community Partner physicians. Some

Community Partners were also nominated by members of the RELIANCE Executive Committee.



Supplemental Figure 1

RELIANCE patient referral



Returning?

AAA



1. PATIENT ELIGIBILITY

I attest that my patient meets ALL of the following inclusion criteria:

a. Patient and treating clinician considering treatment intensification with roflumilast or azithromycin to reduce the risk of COPD exacerbations;

b. Age \geq 40 years;

c. Current or past smoker of at least 10 pack years;

d. Diagnosis of severe COPD and associated chronic bronchitis;

e. Hospitalized with a diagnosis of COPD exacerbation in the past 12 months OR hospitalized with respiratory complications associated with COVID-19 in the past 12 months;

f. Current medications include inhaled LAMA, ICS/LABA, or LAMA/LABA;

g. English or Spanish speaking;

h. Willing and able to provide a contact telephone number.

☒ Agree

☐ Disagree

☐ Unsure - I would like a call back from a RELIANCE clinician

Please enter the date of last hospitalization referenced in item e. above

M-D-Y

2. I attest that my patient meets NONE of the following exclusion criteria:

a. History of intolerance to azithromycin or roflumilast that the patient or patient's treating clinician considers sufficiently serious to avoid either treatment option;

b. Current treatment with long-term (more than 30 days) roflumilast, azithromycin, or ensifentrine;

c. Known hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic;

d. History of cholestatic jaundice/hepatic dysfunction with prior use of azithromycin;

e. Moderate to severe liver impairment (Child-Pugh B or C);

f. Current pregnancy;

g. Any other clinician-determined exclusion as per my clinical practice.

☒ Agree

☐ Disagree

☐ Unsure - I would like a call back from a RELIANCE clinician

3. Confirmation of patient assent to be contacted:

- ☒ I confirm that I have discussed the RELIANCE study with my patient and they would like to be contacted with further information. My patient agrees to be contacted by the Call Center.
- ☐ I confirm that I have discussed the RELIANCE study with my patient. My patient would like to contact the Call Center for further information.

4. Please mail this patient an introductory RELIANCE kit. (This includes an envelope with a study overview, paper consent, and Call Center contact information.)☐**5. PATIENT INFORMATION**

How should the call center reach your patient?

First name	<input type="text" value="John"/>
Last name	<input type="text" value="Doe"/>
Preferred contact phone #	<input type="text" value="(555) 555-5555"/>
Alternate contact phone # (optional)	<input type="text"/>
Email address (optional)	<input type="text"/>
Preferred contact method	<input checked="" type="radio"/> Phone <input type="radio"/> Email
Preferred language	<input checked="" type="radio"/> English <input type="radio"/> Spanish

6. TREATING CLINICIAN INFORMATION

Clinic name	<input type="text" value="University of Illinois at Chicago"/>
Clinician first name	<input type="text" value="Jerry"/>
Clinician last name	<input type="text" value="Krishnan"/>
Preferred contact phone #	<input type="text" value="555-555-5555"/>
Alternate contact phone #	<input type="text" value="555-555-5555"/>
Clinician email	<input type="text" value="sample@uic.edu"/>

7. Is the information above correct?

- ☒ Yes
- ☐ No

8. Comments

Do you have any additional comments?

For example, please include the patient's preferred days or times to be contacted by the study team.

Patient would like to be contacted at 4pm tomorrow (Thursday).

If you have questions and would like to speak to a RELIANCE Coordinator, please call 1-833-687-2673.

If you have questions and would like to speak to a study clinician, please call 312-674-2781.

If you would like more information about RELIANCE, please visit [RELIANCE-Study.org](https://reliance-study.org) or [ClinicalTrials.org](https://clinicaltrials.org) or email reliance@uic.edu.

Submit

Save & Return Later

