NYU Langone Health

Division of Pulmonary and Critical Care Medicine

NTM PATIENT EDUCATION PROGRAM

NTM Clinical Trials at NYU Langone Health

Stephanie Lau, MD

Clinical Assistant Professor of Medicine

NYU Langone Medical Center

Conflict of Interest

- Study Coordinator for the Insmed inhaled liposomal amikacin studies
- Study Coordinator for the Aradigm inhaled ciprofloxacin study
- Study Coordinator for the Insmed Willow Study
- Study Coordinator for the Hillrom Vest study
- Stud Coordinator for the Insmed questionnaire study

NON-PHARMACOLOGIC TRIALS

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Active

NYU Lung and Airways Disease Registry

- All patients with pulmonary disease are enrolled
- Extensive database to follow the natural progression of different pulmonary diseases
- Patient outcomes are analyzed with plans for the development of future clinical trials

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Active

Bronchiectasis Research Registry

- Consolidated database
  - non-cystic fibrosis bronchiectasis
  - non-tuberculous mycobacterial (NTM) lung disease
  - institutions across the country
- Sponsored by the COPD Foundation
- NYU became a part of the registry in 2017
- Objective is to prospectively observe outcomes of patients with bronchiectasis and NTM lung disease
- Promote the development of future clinical trials

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Evaluation of the Lung Microbiome in NTM Bronchiectasis

Active

- Study population:
  - Bronchiectasis
  - NTM lung disease
- Objective: to determine if distinct changes in the lower airway microbiome are associated with changes in the host immune response and development of pulmonary NTM disease
- Collect:
  - induced sputum
  - blood
  - bronchoscopy samples

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Active

Hill Rom Vest Study

- Patients with non-cystic fibrosis bronchiectasis who have ≥ 2 pulmonary exacerbations a year
- Non-blinded, randomized controlled study > efficacy of The Vest® System vs acapella® vibratory PEP device.
- This study is currently enrolling subjects.

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PHARMACOLOGIC TRIALS

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Completed Trials

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Completed

The Pulmaquin Study (ORBIT-4)

- Study population:
  - non-cystic fibrosis bronchiectasis
  - chronic lung infections due to Pseudomonas aeruginosa
- Liposome-encapsulated ciprofloxacin vs placebo for 48 weeks
- Outcome Measures:
  - Primary endpoint: time to first pulmonary exacerbation
  - Secondary endpoint: frequency of pulmonary exacerbations
- Results from ORBIT-3 and ORBIT-4
  - ORBIT-3 did not meet either endpoint while ORBIT-4 did
- Outcome
  - Did not receive FDA approval

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Completed

Arikayce for Nontuberculous Mycobacteria

- Patients with recalcitrant NTM lung disease
- Liposomal Amikacin for Inhalation (LAI) vs placebo
- 84 days with an additional 84 days of open-label

ORIGINAL ARTICLE

Randomized Trial of Liposomal Amikacin for Inhalation in Nontuberculous Mycobacterial Lung Disease

Kenneth N. Olivier[1], David E. Griffith[2], Gina Eagle[3], John P. McGinnis II[3], Liza Micioni[3], Keith Liu[3], Charles L. Daley[4], Kevin L. Winthrop[5], Stephen Ruoss[6], Doreen J. Addrizzo-Harris[7], Patrick A. Flume[8], Daniel Dorgan[9], Matthias Salathe[10], Barbara A. Brown-Elliott[2], Renu Gupta[3,11], and Richard J. Wallace, Jr.[2]

[1]National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland; [2]The University of Texas Health Science Center at Tyler, Tyler, Texas; [3]Insmed Incorporated, Bridgewater, New Jersey; [4]National Jewish Health, Denver, Colorado; [5]Oregon Health & Science University, Portland, Oregon; [6]Stanford University School of Medicine, Stanford, California; [7]New York University School of Medicine, New York, New York; [8]Medical University of South Carolina, Charleston, South Carolina; [9]Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; [10]Leonard M. Miller School of Medicine, University of Miami, Miami, Florida; and [11]Global Biopharma, Moorestown, New Jersey

American Journal of Respiratory and Critical Care Medicine Volume 195 Number 6 | March 15 2017

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Completed

Arikayce for Nontuberculous Mycobacteria

- Results:
  - Primary endpoint of change in baseline to Day 84 on a semiquantitative mycobacterial growth scale was not met.
  - LAI added to a multi-drug regimen resulted in improvement in sputum conversion
  - Led to INS-212 and INS-312 studies

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Completed

The CONVERT Study (INS-212)

- Phase 3 study.
- Patients with refractory Mycobacterium avium complex (MAC) lung disease
- Evaluate the efficacy and safety of LAI added to guideline-based therapy (GBT) vs guideline-based therapy alone
- Primary endpoint: culture conversion by Month 6
- Treated for 12 additional months after sputum conversion (3 consecutive months of sputums negative for MAC).
- If sputum did not convert after 6 months of treatment, option to enroll in INS-312
- Enrollment ended November 2016

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The CONVERT Study (INS-212)

NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

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Format: Abstract Send to

Am J Respir Crit Care Med. 2018 Sep 14. doi: 10.1164/rccm.201807-1318OC. [Epub ahead of print]

Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by Mycobacterium avium Complex (CONVERT): A Prospective, Open-Label, Randomized Study.

Griffith DE[1], Eagle G[2], Thomson R[3,4], Aksamit TR[5], Hasegawa N[6], Morimoto K[7], Addrizzo-Harris DJ[8], O'Donnell AE[9], Marras TK[10], Flume PA[11], Loebinger MR[12], Morgan L[13], Codecasa LR[14], Hill AT[15], Ruoss SJ[16], Yim JJ[17], Ringshausen FC[18], Field SK[19], Philley JV[20], Wallace RJ Jr[21], van Ingen J[22], Coulter C[23], Nezamis J[2], Winthrop KL[24]; CONVERT Study Group.

Author information

Abstract

Rationale Improved therapeutic options are needed for patients with treatment-refractory nontuberculous mycobacterial lung disease caused by Mycobacterium avium complex (MAC). Objectives To evaluate the efficacy and safety of daily amikacin liposome inhalation suspension (ALIS) added to standard guideline-based therapy (GBT) in patients with refractory MAC lung disease. Methods Adults with amikacin-susceptible MAC lung disease and MAC-positive sputum cultures despite ≥6 months of stable GBT were randomly assigned (2:1) to receive ALIS with GBT (ALIS+GBT) or GBT alone. Once-daily ALIS was supplied in single-use vials delivering 590 mg amikacin to the nebulizer. The primary endpoint was culture conversion, defined as 3 consecutive monthly MAC-negative sputum cultures by month 6. Measurements and Main Results Enrolled patients (ALIS+GBT, n=224; GBT-alone, n=112) were a mean 64.7 years old and 69.3% female. Most had underlying bronchiectasis (62.5%), chronic obstructive pulmonary disease (14.3%), or both (11.9%). Culture conversion was achieved by 65 of 224 patients (29.0%) with ALIS+GBT and 10 of 112 (8.9%) with GBT alone (OR, 4.22; 95% CI [2.08, 8.57]; P<0.001). Patients in the ALIS+GBT arm vs GBT alone were more likely to achieve conversion (hazard ratio, 3.90; 95% CI, [2.00, 7.60]). Respiratory adverse events (primarily dysphonia, cough, and dyspnea) were reported in 87.4% of patients receiving ALIS+GBT and 50.0% receiving GBT alone; serious treatment-emergent adverse events occurred in 20.2% and 17.9% of patients, respectively. Conclusions Addition of ALIS to GBT for treatment-refractory MAC lung disease achieved significantly greater culture conversion by month 6 than GBT alone, with comparable rates of serious adverse events. Clinical trial registration available at www.clinicaltrials.gov, ID NCT02344004.

KEYWORDS: LAI, ALIS; Nontuberculous mycobacteria; culture conversion; guideline-based therapy; liposomal amikacin for inhalation

PMID: 30216086 DOI: 10.1164/rccm.201807-1318OC

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Completed

The CONVERT Study (INS-212)

- Culture conversion was achieved in 29% of patients on LAI + GBT vs 8.9% GBT alone

- The addition of LAI to GBT for treatment-refractory MAC lung disease achieved significantly greater sputum culture conversion by month 6 than GBT alone

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Insmed Announces FDA Approval of ARIKAYCE® (amikacin liposome inhalation suspension), the First and Only Therapy Specifically Indicated for the Treatment of Mycobacterium Avium Complex (MAC) Lung Disease in Adult Patients with Limited or No Alternative Treatment Options

September 28, 2018

—Commercial availability expected in early Q4 2018—

—Conference call scheduled for today at 6:15 PM ET—

BRIDGEWATER, N.J., Sept. 28, 2018 (GLOBE NEWSWIRE) -- Insmed Incorporated (Nasdaq:INSM), a global biopharmaceutical company focused on the unmet needs of patients with rare diseases, today announced that the U.S. Food and Drug Administration (FDA) has granted accelerated approval of ARIKAYCE® (amikacin liposome inhalation suspension) for the treatment of *Mycobacterium avium* complex (MAC) lung disease as part of a combination antibacterial drug regimen for adult patients who have limited or no alternative treatment options. ARIKAYCE is the first and only therapy approved in the U.S. specifically for patients with MAC lung disease, a chronic and debilitating condition that can significantly increase patient morbidity and mortality.

ARIKAYCE is the first product approved via the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD). LPAD, which was enacted as part of the 21st Century Cures Act, serves to advance the development of new antibacterial drugs to treat serious or life-threatening infections in limited populations of patients with unmet needs.

"Today's approval is a momentous occasion for all of us living with and advocating for people with MAC lung disease," said Philip Leitman, President of

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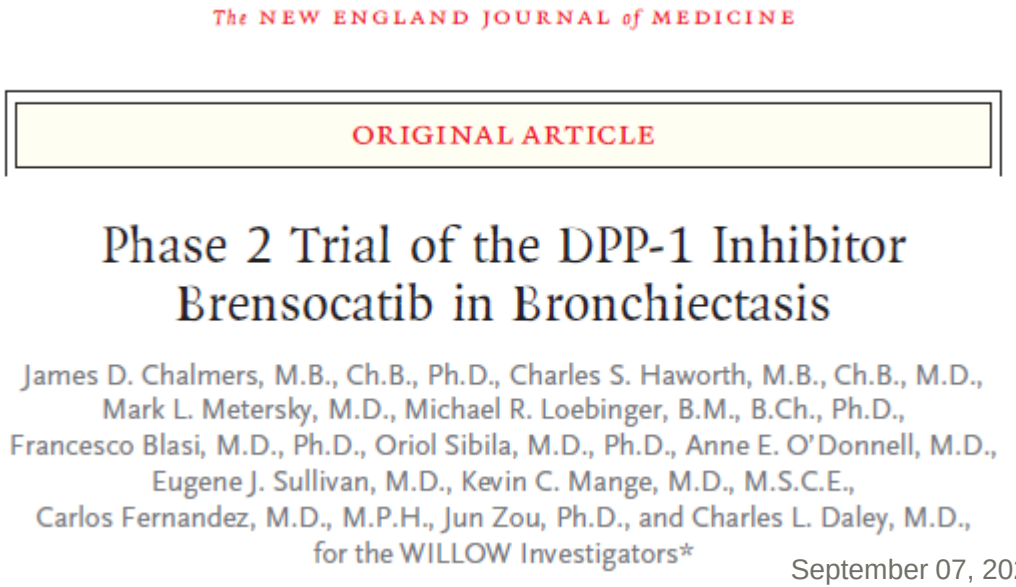
Completed

Willow

- Patients with non-cystic fibrosis bronchiectasis with frequent pulmonary exacerbations
- Study drug: Brensocatib (INS1007)
  - anti-inflammatory pill taken once a day for 24 weeks



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 2 Trial of the DPP-1 Inhibitor Brensocatib in Bronchiectasis

James D. Chalmers, M.B., Ch.B., Ph.D., Charles S. Haworth, M.B., Ch.B., M.D., Mark L. Metersky, M.D., Michael R. Loebinger, B.M., B.Ch., Ph.D., Francesco Blasi, M.D., Ph.D., Oriol Sibila, M.D., Ph.D., Anne E. O'Donnell, M.D., Eugene J. Sullivan, M.D., Kevin C. Mange, M.D., M.S.C.E., Carlos Fernandez, M.D., M.P.H., Jun Zou, Ph.D., and Charles L. Daley, M.D., for the WILLOW Investigators*

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Completed

Willow

- Treatment with Brensocatib compared to placebo led to:
  - Prolonged time to first exacerbation
  - 40% reduction in risk of exacerbation
  - Lower exacerbation rate

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Active Trials

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Active

PROMIS II

- Phase 3 study.
- Patients with non-cystic fibrosis bronchiectasis with frequent pulmonary exacerbations due to Pseudomonas aeruginosa
- Randomized, double-blind, placebo-controlled study
- Study drug: colistimethate sodium (Promixin®)
  - antibiotic
  - inhaled twice daily via I-neb
- Co-primary endpoints: annualized pulmonary exacerbation rate and annualized number of pulmonary exacerbation-free days
- Treat for 12 months
- Currently enrolling at our site

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Active

MAC 2 vs 3

- Patients with non-cystic fibrosis bronchiectasis who have MAC lung disease, which has never been treated and will need to start therapy
- Randomized study:
  - azithromycin + ethambutol (2-drug therapy) vs azithromycin + ethambutol + rifampin (3-drug therapy)
- Primary endpoints:
  - to determine if 2-drug therapy is non-inferior to 3-drug therapy in the treatment of pulmonary MAC
  - to determine whether 2-drug therapy is better tolerated than 3-drug therapy
- Treat for 12 months, three days a week therapy
- Currently enrolling

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Active

Insmed Patient Reported Outcomes Study in NTM

- Patients with non-tuberculous mycobacterium (NTM) lung infections due to Mycobacterium avium complex (MAC) and Mycobacterium abscessus who are symptomatic
- Conduct interviews to collect information on patient symptoms in order to develop new patient reported outcome (PRO) tools .
- These new PRO tools can then be used in clinical trials to help evaluate treatment efficacy.
- This study is currently enrolling subjects.

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Upcoming Trials

Upcoming

Arikayce INS-416 and INS-415

- Patients with non-tuberculous mycobacterium (NTM) lung infections due to Mycobacterium avium complex (MAC) who are starting treatment.
- Randomized, double-blind, placebo-controlled study > safety and efficacy of Arikayce + azithromycin + ethambutol vs placebo + azithromycin + ethambutol.
- Conduct interviews to collect information on patient symptoms in order to develop new patient reported outcome (PRO) tools .
- This study is not yet open to enrollment.

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Upcoming

The Aspen Study INS-301

- Patients with non-cystic fibrosis bronchiectasis who have ≥ 2 pulmonary exacerbations a year
- Randomized, double-blind, placebo-controlled study > safety, tolerability and efficacy of Brensocatib 10 mg and 25 mg.
- This study is not yet open for enrollment.

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Insmed Patient Reported Outcomes Study in Bronchiectasis

Upcoming

- Patients with non-Cystic Fibrosis bronchiectasis with or without non-tuberculous mycobacterium (NTM) lung infections due to Mycobacterium avium complex (MAC) and Mycobacterium abscessus who are symptomatic
- Conduct interviews to collect information on patient symptoms in order to develop new patient reported outcome (PRO) tools .
- These new PRO tools can then be used in clinical trials to help evaluate treatment efficacy.
- This study is not yet open for enrollment.

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Interested in Participating in Clinical Research?

Call 212-263-7951

Stephanie Lau, MD

NYU Langone Health

THANK YOU

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