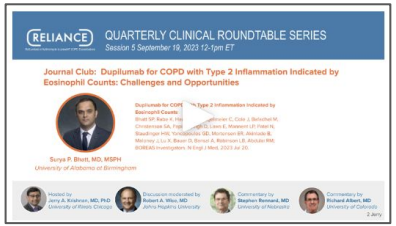
QUARTERLY CLINICAL ROUNDTABLE SERIES

RofLumilast or Azithromycin to preveNT COPD Exacerbations

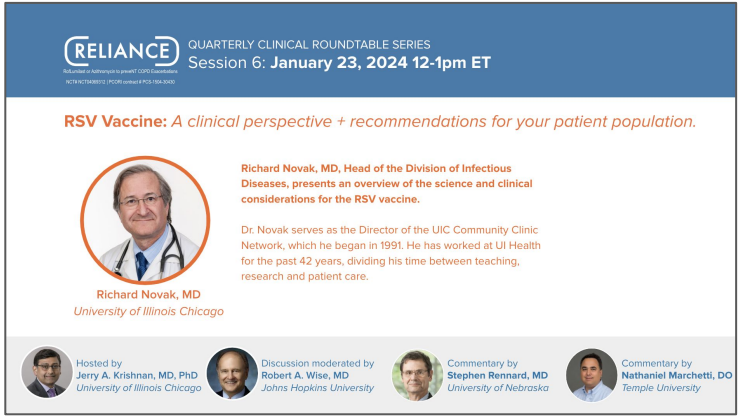
April 5, 2022 | Preventing COPD exacerbations: talking to patients and experts about deciding between medicines.

July 26, 2022 | How to be successful Clinical Centers or Community Partners in RELIANCE

June 13, 2023 | Journal Club: Use of roflumilast in your patient population



September 19, 2023 | Journal Club: Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts



Watch past events at
reliance-study.org/clinicians/#roundtable

Have an idea for a roundtable?
Put it in the chat!

1 Jerry

RELIANCE
RofLumilast or Azithromycin to preveNT COPD Exacerbations
NCT# NCT04069312 | PCORI contract # PCS-1504-30430

QUARTERLY CLINICAL ROUNDTABLE SERIES
Session 6: **January 23, 2024 12-1pm ET**

RSV Vaccine: *A clinical perspective + recommendations for your patient population.*

Richard Novak, MD
University of Illinois Chicago

Richard Novak, MD, Head of the Division of Infectious Diseases, presents an overview of the science and clinical considerations for the RSV vaccine.

Dr. Novak serves as the Director of the UIC Community Clinic Network, which he began in 1991. He has worked at UI Health for the past 42 years, dividing his time between teaching, research and patient care.

Hosted by
Jerry A. Krishnan, MD, PhD
University of Illinois Chicago

Discussion moderated by
Robert A. Wise, MD
Johns Hopkins University

Commentary by
Stephen Rennard, MD
University of Nebraska

Commentary by
Nathaniel Marchetti, DO
Temple University

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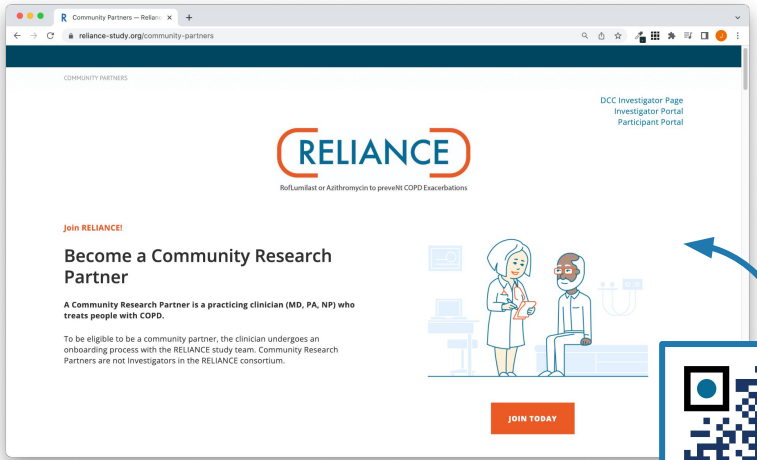
RofLumilast or Azithromycin to preveNT COPD Exacerbations

QUARTERLY CLINICAL ROUNDTABLE SERIES

Session 5 September 19, 2023 12-1pm ET

1. Please mute yourself
2. **Put questions + comments in the chat**
3. Consider joining RELIANCE,
   or tell a colleague!
   a. Pragmatic clinical trial embedded in clinical practice, funded by PCORI
   b. Long-term azithromycin vs. roflumilast in patients with COPD associated with chronic bronchitis
   c. N=631 enrolled as of 1/21/2024
   d. ClinicalTrials.gov: NCT04069312

Learn more about RELIANCE and how to join
https://www.reliance-study.org/community-partners



RELIANCE

Richard Novak, MD

University of Illinois Chicago

Harry F. Dowling Professor and Chief
Division of Infectious Diseases

RSV Prevention

Richard Novak, MD
Harry F. Dowling Professor and Chief
Division of Infectious Diseases
University of Illinois at Chicago

What is RSV and who is at risk?

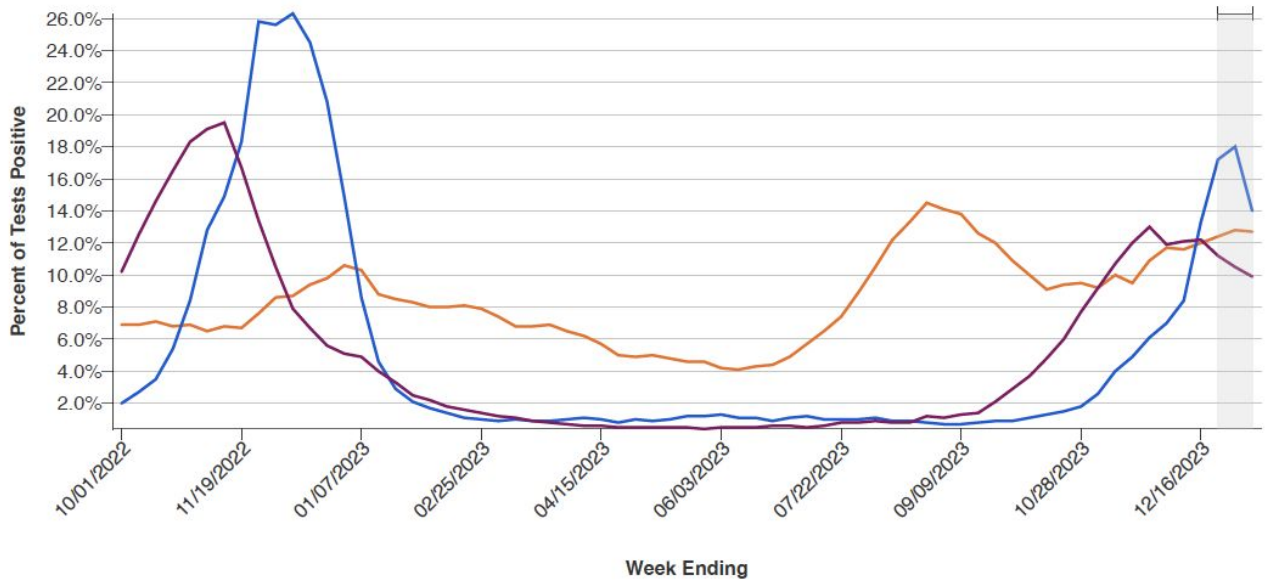
- enveloped, negative-sense, single-stranded RNA virus
- Two subtypes of RSV
  - RSV Type A (RSV-A)
  - RSV Type B (RSV-B)
  - Usually, one of the two are dominant each year

Who is at Risk?

- causes seasonal infections in a biphasic age distribution
- Most often affects children up to age 2 years
  - Infancy under 3 months of age
  - Prematurity, Down’s syndrome. Neuromuscular diseases
  - Pediatric cardiopulmonary diseases
- older adults
  - Aging, immune senesence
  - medical immunosuppression
  - Incidence similar to influenza in season

Respiratory Virus Activity Levels

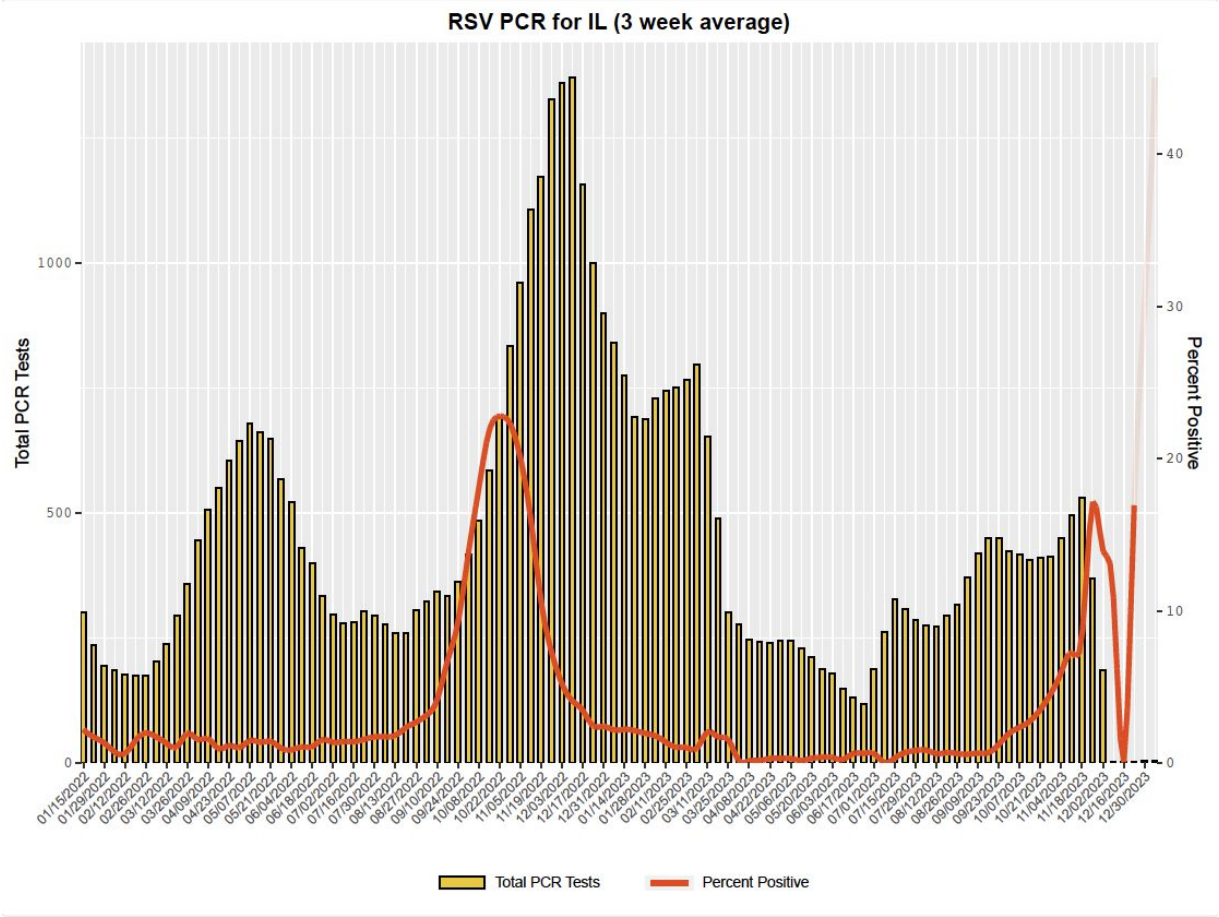
Weekly percent of tests positive for the viruses that cause COVID-19, influenza, and RSV at the national level. Preliminary data are shaded in gray.



Data presented through: 01/06/2024; Data as of: 01/11/2024

CDC.gov

RSV Testing Trends, Illinois



CDC.gov

Disease manifestations

- Upper respiratory tract disease
- Lower respiratory tract disease
- Children
  - Bronchiolitis
  - Pneumonia
  - Second leading cause of death in children, 99% in resource poor countries
- Adults
  - Bronchiolitis and pneumonia
  - Exacerbations of COPD or heart failure

Is there natural immunity?

- Exposure and reinfection recurs throughout life
- Natural immunity is incomplete, does not protect against subsequent infections

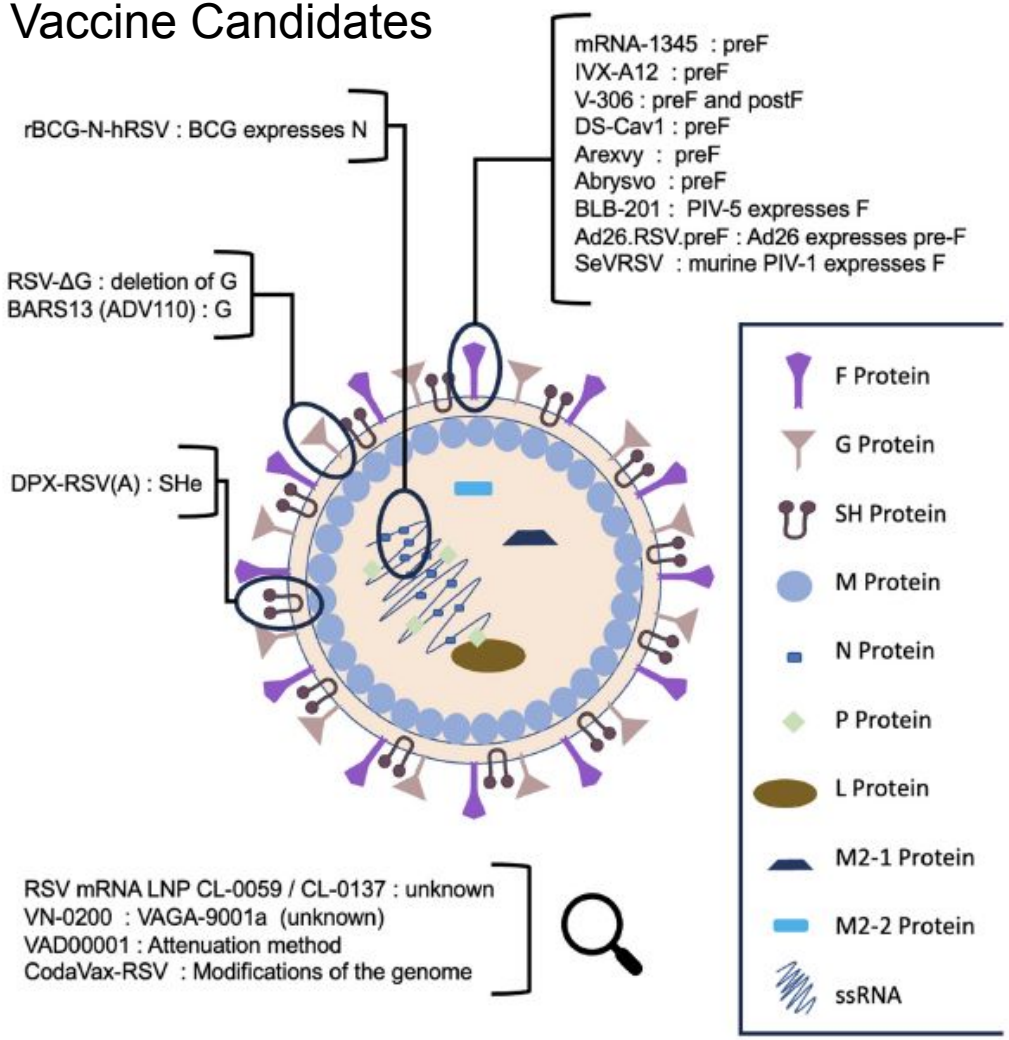
RSV Vaccine History

- First attempted in the 1960's
- Formalin inactivated RSV
- Enhanced Respiratory Disease
  - Poor antibody response
  - TH2 response to vaccine: immunosuppressive effect
  - Subsequent research focused on increased antibody response without TH2 effect

Current RSV Vaccine Development

- 24 vaccines in development, 2 licensed
- Most target the stabilized Pre Fusion Protein, F
  - Virus uses this to attach to host cells
- Many different vaccine delivery strategies are in use
  - mRNA
  - Vector
  - Subunit
  - Live, attenuated

RSV Vaccine Candidates



Topalidou, et al, 2023

ABRYSVO (Pfizer)

- Bivalent stabilized preF subunit vaccine: Subgroups A and B
- Single IM dose
- Phase 3, randomized placebo controlled trial in adults > age 60 (Renoir)
  - 34,284 enrolled
  - Primary endpoint was incident lower respiratory tract disease with
    - At least 2 symptoms: cough, wheezing, sputum production, shortness of breath, or tachypnea
    - Positive PCR test for RSV
- Study stopped early with 7 months of observation
- 11 participants in the vaccine group (1.19 cases per 1000 person-years of observation) and 33 participants in the placebo group (3.58 cases per 1000 person-years of observation)
- vaccine efficacy, 66.7%; confidence interval 28.8 to 85.8)
- Safety: injection site pain, systemic reactions no different than placebo

ABRYSVO (Pfizer) in Pregnant women (Matisse trial)

- phase 3, double-blind placebo-controlled trial in 18 countries
- pregnant women at 24 through 36 weeks gestation to receive a single intramuscular injection
- two primary efficacy end points:
  - medically attended severe RSV-associated lower respiratory tract illness and
  - medically attended RSV-associated lower respiratory tract illness in infants within 90, 120, 150, and 180 days after birth
- 3682 maternal participants received vaccine and 3676 received placebo; 3570 and 3558 infants, respectively, were evaluated
- severe lower respiratory tract illness occurred within 90 days after birth in 6 infants of women in the vaccine group and 33 infants of women in the placebo group (vaccine efficacy, 81.8%; 99.5% CI, 40.6 to 96.3)
- 19 cases and 62 cases, respectively, occurred within 180 days after birth (vaccine efficacy, 69.4%; 97.58% CI, 44.3 to 84.1).

AREXVY (GSK)

- Monovalent Pre fusion subunit vaccine with $AS01_E$ adjuvant
- Phase 3 placebo-controlled trial in adults > age 60
- 24,996 participants, median follow-up of 6.7 months
- vaccine efficacy against RT-PCR–confirmed RSV-related lower respiratory tract disease was 82.6% (confidence interval 57.9 to 94.1),
- 7 cases (1.0 per 1000 participant-years) in the vaccine group and 40 cases (5.8 per 1000 participant-years) in the placebo group.
- Equally efficacious against Subgroups A and B
- Safety: injection site pain, mild fatigue (33% vs 16% placebo), resolved in 1-2 days

Ad26.RSV.preF-RSV preF Protein Vaccine (Janssen)

- randomized, double-blind, placebo-controlled, phase 2b, proof-of-concept trial to evaluate the efficacy
- Adults aged ≥ 65, three case definitions
- 5592 participants, 2791 received vaccine and 2801 received placebo
- Vaccine efficacy was 80.0% (94.2% confidence interval [CI], 52.2 to 92.9), 75.0% (94.2% CI, 50.1 to 88.5), and 69.8% (94.2% CI, 43.7 to 84.7) depending on case definition
- Safety: 41.4% for vaccine and by 16.4% placebo; The most common systemic adverse events included fatigue, headache, and myalgia

RSV Prevention Guidelines

- Adults > age 60
- Pregnant women in their third trimester of pregnancy

- Children < 8 mo age:
  - Monoclonal antibody infusion
  - 2 available products
    - Nirsevimab (Beyfortus)
    - Palivizumab (Synagis)
  - Not indicated if mother was vaccinated in last trimester, unless child was born <14 days after RSV vaccination

RELIANCE Q&A

Robert A. Wise, MD
Johns Hopkins University

Attendees:

Add questions or your feedback on today's roundtable in the chat.

***Become a Community Partner: Complete a brief form** to nominate yourself or a colleague to learn more, or point your phone camera at the QR code.*

20 Bob

RELIANCE Commentary

Stephen Rennard, MD
University of Nebraska

Nathaniel Marchetti, DO
Temple University

Attendees:

Add questions, feedback on today's roundtable, or topic requests for the next roundtable in the chat.

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Thank you!