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Arexvy's effectiveness over two consecutive RSV seasons

Submission date	Recruitment status	[_] Prospectively registered
06/08/2026	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/08/2026	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
25/08/2026	Infections and Infestations	[X] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Principal investigator, Scientific, Public

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Additional identifiers

Study information

Scientific Title
Effectiveness of Arexvy in preventing RSV-associated hospitalizations and complications among US adults over two consecutive seasons

Study objectives
In June 2023, the Centers for Disease Control and Prevention (CDC) recommended a single dose of RSV vaccine for prevention of RSV-associated, lower respiratory tract disease (LRTD) among

adults aged ≥60 years using shared clinical decision-making. In June 2024, the single-dose vaccine recommendation was updated as a universal recommendation for all adults aged ≥75 years and a risk-based recommendation for those aged 60–74 years who are at increased risk for severe RSV disease. There are three vaccines against RSV currently licensed and recommended for use in the US. All vaccines target the highly conserved RSV prefusion F protein. Two of these vaccines, GSK's Arexvy® and Pfizer's Abrysvo®, are protein subunit vaccines and were recommended for use in 2023; a third vaccine, Moderna's mRESVIA®, an mRNA vaccine, was recommended for use in 2024.

Initial evaluations by our group and others have demonstrated the effectiveness of a single RSV vaccine dose in preventing hospitalizations for RSV and related complications. Extended follow-up of prelicensure clinical trials has documented sustained protection against RSV LRTD over 2–3 seasons. However, none of those prelicensure RSV vaccine trials were designed or powered to estimate efficacy against RSV-associated hospitalization or related severe in-hospital outcomes, and those studies underrepresented or excluded relevant vulnerable groups, including adults aged ≥75 years and those with chronic medical conditions, including immunocompromising conditions. New comprehensive studies examining the durability of the protection of the initial RSV vaccination among older adults, including clinically relevant severe endpoints, and examination of vaccine effectiveness (VE) among vulnerable groups are warranted.

Between 2019 and 2025, the Investigating Respiratory Viruses in the Acutely Ill (IVY) Network examined the effectiveness of vaccines in preventing hospitalizations for acute respiratory infections and their complications among US adults. This large multicenter network prospectively enrolled adults hospitalized with acute respiratory illnesses and applied a test negative/case-control design for vaccine effectiveness (VE) assessments. IVY has continuously compiled detailed information that enables studies of RSV vaccine effectiveness through 2025, including two RSV seasons after the first recommendation of RSV vaccines for US adults. We propose to leverage data from the IVY research platform to expand initial assessments of the effectiveness of Arexvy against RSV-associated hospitalization among adults, by addressing the following objectives:

Primary objectives:
1. Estimate the (pooled) single-season effectiveness of one dose of Arexvy against RSV-associated hospitalization among adults aged 60 years or older, encompassing two consecutive RSV seasons. This will be computed overall and by:
1.1. Comorbidities: adults with up to one, two, three or more chronic respiratory (e.g., chronic obstructive pulmonary disease [COPD]/asthma), cardiovascular, or other chronic conditions (including diabetes, chronic kidney disease [CKD], chronic liver disease, obesity, neurological conditions, among others)
1.2. Immunosuppression (based on underlying conditions or use of immunosuppression-inducing medications) and encompassing B-cell dysfunction, solid organ or hematopoietic stem-cell transplantation (HSCT), AIDS, malignancy, autoimmune or autoinflammatory disease, or other immunosuppressive conditions (e.g., CKD).
1.3. Frailty surrogate indicators: derived through a combination of age, healthcare utilization history (including hospitalizations and emergency department visits during the prior year), comorbidities, and available information on residence prior to hospitalization (e.g., home, skilled nursing facility, etc).

Secondary objectives:
1. Estimate the effectiveness of one dose of Arexvy against RSV-associated hospitalization among adults aged 60 years or older over two seasons overall and by:
1.1. Comorbidities: adults with up to one, two, three or more chronic respiratory (e.g., COPD

/asthma), cardiovascular, or other chronic conditions (including diabetes, CKD, chronic liver disease, obesity, neurological conditions, among others)
1.2. Immunosuppression (based on underlying conditions or use of immunosuppression-inducing medications) encompassing B-cell dysfunction, solid organ or hematopoietic stem-cell transplantation (HSCT), AIDS, malignancy, autoimmune or autoinflammatory disease, or other immunosuppressive conditions (e.g., CKD).
1.3. Frailty surrogate indicators: derived through a combination of age, healthcare utilization history (including hospitalizations and emergency department visits during the prior year), comorbidities, and available information on residence prior to hospitalization (e.g., home, skilled nursing facility, etc).
2. Estimate the seasonal effectiveness and the effectiveness over two seasons of one dose of Arexvy against RSV-associated severe hospitalization (defined as a composite of acute respiratory or organ failure (including need for ventilatory or other organ support, e.g., supplemental oxygen, ECMO, among others), intensive care unit (ICU) admission or death) among adults aged 60 years or older.
3. Estimate the seasonal effectiveness and the effectiveness over two seasons of one dose of Arexvy against RSV-associated hospitalization among adults aged 60 years or older over two RSV seasons by: age group: adults aged 60 to 74 years and 75 years or older

Exploratory objectives:
1. Explore the durability of vaccine protection by examining the influence of time since vaccination evaluating continuous time (in days) elapsed since vaccination through illness onset (overall and in subgroups as sample size would allow).
2. Explore the influence of vaccination on loss of independence indicators, such as post-discharge disposition information (e.g., transition from home community dwelling at admission to a skilled nursing facility at discharge).

The pooled singleseason vaccine effectiveness (VE) refers to the effectiveness of an RSV vaccine dose during the season in which it was given, pooled across vaccination years. For each season (2023-2024 and 2024-2025), this assessment will include vaccinations and RSV-related hospitalizations that occurred in the same season. These VE estimates will be computed overall and by factors listed in the respective objectives.

The VE over two seasons refers to the effectiveness of one RSV vaccine dose given in the 2023-2024 season and will be assessed, including RSV-related hospitalizations that occurred during the 1 October 2023 to 30 April 2025 period. These VE estimates will be computed overall and by factors listed in the respective objectives.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 13/07/2026, Vanderbilt University Medical Center Human Research Protections Program (2525 West End Avenue Suite 600, Nashville, 37203, United States of America; +1 (0) 615 322 2918; kyle.rybczyk@vumc.org), ref: 260776

Primary study design
Observational

Secondary study design
Test-negative design

Study type(s)

Health condition(s) or problem(s) studied
Respiratory syncytial virus (RSV) infection

Interventions
This study will only examine Arexvy vaccines. We will first define vaccination status among hospitalized patients as follows: 1) unvaccinated, defined as no prior receipt of RSV vaccination or RSV vaccination after illness onset, and 2) vaccinated, defined as receipt of a single dose of RSV vaccine ≥14 days before illness onset. Patients who received more than one RSV vaccine dose or received RSV vaccine <14 days before illness onset will be excluded. These definitions with RSV vaccination history, will be used for the assessments of VE in this project.

To assess the pooled seasonal (single season) Arexvy VE, RSV vaccinations will be characterized based on timing of vaccination in the same season relative to illness onset. For each RSV season, same season of RSV vaccination will be defined as Arexvy vaccinations that occurred from 1 August 2023 through 31 March 2024 for patients hospitalized during 1 October 2023 through 31 March 2024 or as RSV vaccinations that occurred from 1 August 2024 through 30 April 2025 for patients hospitalized during 1 October 2024 through 30 April 2025.

For the assessment of Arexvy effectiveness over two RSV seasons, Arexvy vaccinations will be defined as those that occurred from 1 August 2023 through 31 March 2024 for patients hospitalized from 1 October 2023 through 30 April 2025.

In a separate exploratory analysis, we will assess the durability of Arexvy protection based on time since RSV vaccination.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Arexvy

Primary outcome(s)
1. Laboratory-confirmed RSV-associated hospitalization measured using RT-PCR of respiratory specimens at the 2023-2024 and 2024-2025 RSV season

Key secondary outcome(s)
1. RSV-associated severe hospitalization measured using a composite of acute respiratory or organ failure (including need for ventilatory or other organ support e.g., supplemental oxygen, ECMO, among others), intensive care unit (ICU) admission or death, at the 2023-2024 and 2024-2025 RSV season

Completion date
31/07/2027

Eligibility

Key inclusion criteria
The proposed study will be restricted to enrolled adults 60 years and older who were hospitalized with ARI during 1 October 2023 to 30 April 2025 and had clinical testing for RSV, SARS-CoV-2, or influenza within 10 days of illness onset and 3 days of hospital admission. Patients who tested positive for RSV only will be considered RSV cases, and patients who tested negative for RSV, SARS-CoV-2 and influenza will be considered controls. Patients who had negative clinical viral testing and subsequently tested positive for RSV on central testing will be included as RSV cases.

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
60 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
8725

Key exclusion criteria
Patients who received other non-Arexvy RSV vaccines during the study period

Date of first enrolment
01/10/2023

Date of final enrolment
30/04/2025

Locations

Countries of recruitment
United States of America

Sponsor information

Organisation
Vanderbilt University Medical Center

ROR
https://ror.org/05dq2gs74

Funder(s)

Funder type

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available