The efficacy of a single dose of the respiratory syncytial virus prefusion F protein vaccine in adults ≥60 years of age over 3 RSV seasons

Michael G. Ison, Alberto Papi, Eugene Athan, Robert G. Feldman, Joanne M. Langley, Dong-Gun Lee, Isabel Leroux-Roels, Federico Martinon-Torres, Tino F. Schwarz, Richard N. van Zyl-Smit, Susanna Cuadripani, Quentin Deraedt, Nancy Dezutter, Catherine Gerard, Laurence Fissette, Stebin Xavier, Aurélie Olivier, Marie Van der Wielen, Dominique Descamps, on behalf of the AReSVi-006 study group

A single dose of RSVPreF3 OA provides protection against RSV-LRTD in older adults over 3 RSV seasons and has an acceptable safety profile.

Background

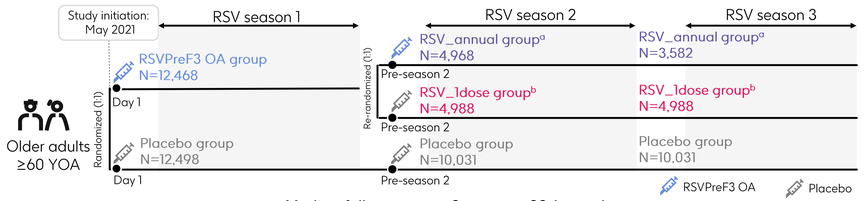
- Respiratory syncytial virus (RSV) infection causes a substantial burden of disease and mortality in older adults.[1]
- Risk factors for severe RSV disease include older age, comorbidities, and immunocompromising conditions.[2]
- The AS01$_E$-adjuvanted RSV prefusion F protein vaccine (RSVPreF3 OA, *Arexvy*, GSK) is approved in several countries for the prevention of RSV-related lower respiratory tract disease (RSV-LRTD) in adults ≥60 years of age (YOA)[3-7] and adults 50–59 YOA at increased risk for RSV-LRTD.[3,8]
- In a study conducted across 17 countries in the Northern Hemisphere (NH) and Southern Hemisphere (SH), a single RSVPreF3 OA dose showed high efficacy against RSV-LRTD (82.6% over 1 RSV season and 67.2% over 2 seasons), severe RSV-LRTD (94.1% and 78.8%), and RSV-related acute respiratory illness (RSV-ARI, 71.7% and 52.7%) in adults ≥60 YOA.[9,10] Efficacy was also observed in participants with comorbidities, including cardiorespiratory conditions.

Purpose

We now report the persistence of vaccine efficacy (VE) of a single RSVPreF3 OA dose over 3 RSV seasons.

Methods

AReSVi-006 trial: phase 3, randomized, double-blind, placebo-controlled, multi-country efficacy study (NCT04886596)



Median follow-up over 3 seasons: 30.6 months

Confirmatory primary objective: VE against RSV-LRTD during RSV season 1[9]

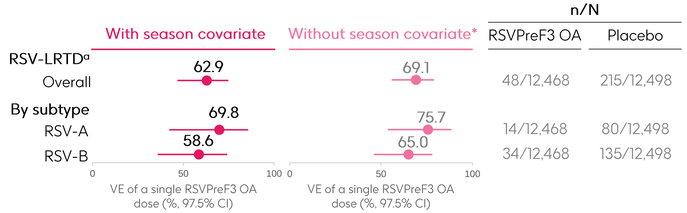
Confirmatory secondary objectives: VE against RSV-LRTD overall over 2 RSV seasons post-dose 1[10] and VE against RSV-LRTD overall and by RSV subtype over 3 seasons (presented here)

Other secondary objectives: VE against severe RSV-LRTD, RSV-LRTD by age, baseline comorbidity and frailty status, VE against RSV-ARI, and safety

Note: RSV season was defined as 1 Oct to 30 Apr in the NH and 1 Mar to 30 Sep in the SH. [a]Annual revaccination evaluation (data not presented here): RSVPreF3 OA group vs Placebo group, participants from the RSV_1dose group contributed to season 1 data only and were censored before administration of dose 2. [b]Single dose evaluation: RSVPreF3 OA group vs Placebo group, participants from the RSV_annual group contributed to season 1 data only and were censored before administration of dose 2; N, number of participants in the modified exposed set (RSV season 1), dose 2-modified exposed set (season 2), participants in the dose 2-modified exposed set who did not receive dose 3 (RSV_annual group) and dose 2-modified exposed set (RSV_1dose and Placebo groups) (season 3).

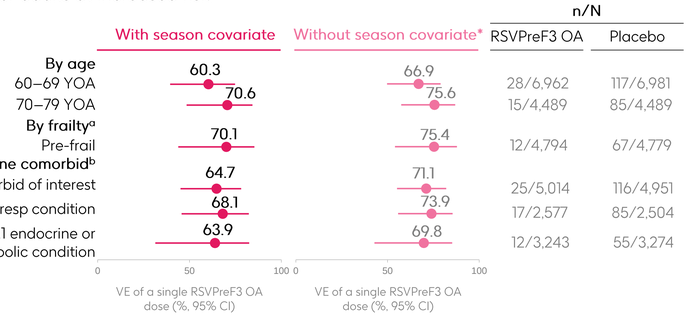
Results

- Demographic characteristics were balanced between groups.
- Significant VE was observed over 3 RSV seasons against RSV-LRTD, regardless of RSV subtype.



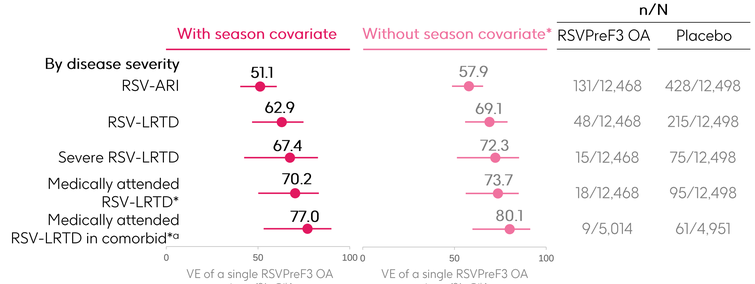
*Post-hoc analysis. [a]Case definition of RSV-LRTD: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours, with ≥1 RSV-positive swab detected by quantitative reverse transcriptase–polymerase chain reaction. Success criteria for confirmatory objectives (lower limit of CI >20% [RSV-LRTD, overall] or >0% [RSV-LRTD, by subtype]). n, number of participants with ≥1 RSV-LRTD; N, number of participants in the modified exposed set.

- VE of a single dose of RSVPreF3 OA was observed over 3 RSV seasons against RSV-LRTD in older adults at increased risk.



Note: Due to too few cases and the low number of participants, VE could not be reliably estimated in adults ≥80 YOA (5/1,017 in RSVPreF3 OA vs 13/1,028 in Placebo) and frail adults (2/189 in RSVPreF3 OA vs 1/176 in Placebo). *Post-hoc analysis. [a]Assessed using a gait speed test: walking speed 0.4–0.99 m/s (pre-frail) and <0.4 m/s or not able to perform the test (frail). [b]Comorbidities of interest included cardiorespiratory conditions (COPD, asthma, any chronic respiratory/pulmonary disease, chronic heart failure) and endocrine or metabolic conditions (diabetes mellitus type 1/2 and advanced liver/renal disease). n, number of participants with ≥1 RSV-LRTD; N, number of participants in the modified exposed set.

- VE was observed over 3 RSV seasons across the clinical spectrum of RSV disease.



*Post-hoc analysis. [a]In participants with ≥1 comorbid of interest, i.e., COPD, asthma, any chronic respiratory/pulmonary disease, chronic heart failure, diabetes mellitus type 1/2 or advanced liver/renal disease. [b]97.5% CI for RSV-LRTD, 95% CI for other endpoints. n, number of participants with ≥1 event; N, number of participants in the modified exposed set.

- VE against RSV-LRTD was observed for each RSV season despite a decreasing VE trend over time.
- The frequency of serious adverse events and potential immune-mediated diseases remained low and balanced across groups through the study.

Conclusions and clinical implications

A single dose of RSVPreF3 OA provides protection against RSV disease over 3 RSV seasons in adults ≥60 YOA, regardless of RSV subtype, disease severity (RSV-LRTD, severe RSV-LRTD, and RSV-ARI), baseline comorbidities, or age, and in pre-frail participants.

RSVPreF3 OA had an acceptable safety profile over 3 seasons, with no cases of Guillain-Barré syndrome or acute disseminated encephalomyelitis reported.

These data support a favorable benefit-risk profile of RSVPreF3 OA over 3 RSV seasons.

Abbreviations

CI, confidence interval; cardioresp, cardiorespiratory; comorbid, comorbidity; COPD, chronic obstructive pulmonary disease.

Affiliations, AReSVi-006 Study Group, References, Disclosures

Click for details.

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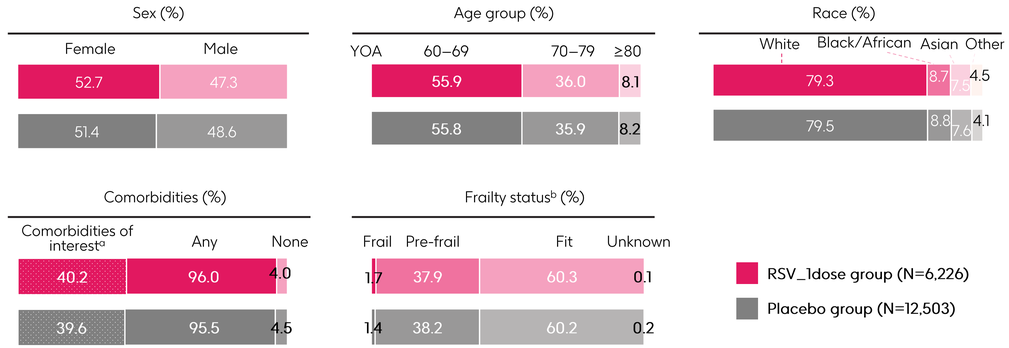
Supplementary material

Main page

Demographic characteristics



[a]Comorbidities of interest included chronic obstructive pulmonary disease (COPD), asthma, any chronic respiratory/pulmonary disease, chronic heart failure, diabetes mellitus type 1/2, and advanced liver/renal disease.
[b]Assessed using a gait speed test: walking speed <0.4 m/s or not able to perform the test (frail), walking speed 0.4–0.99 m/s (pre-frail), walking speed ≥1 m/s (fit). YOA, years of age; N, number of participants in the exposed set (dose 1).

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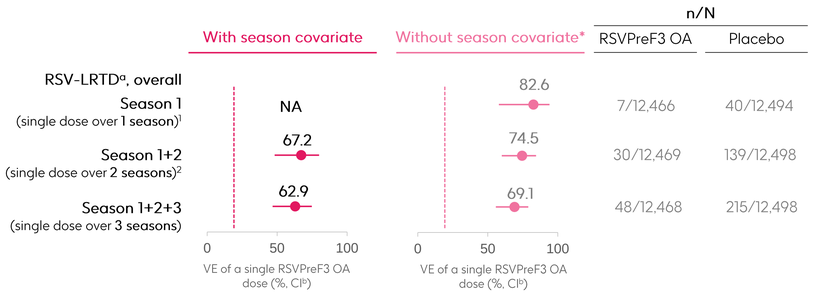
Supplementary material

Main page

VE of a single dose of RSVPreF3 OA against RSV-LRTD over 1, 2, and 3 RSV seasons

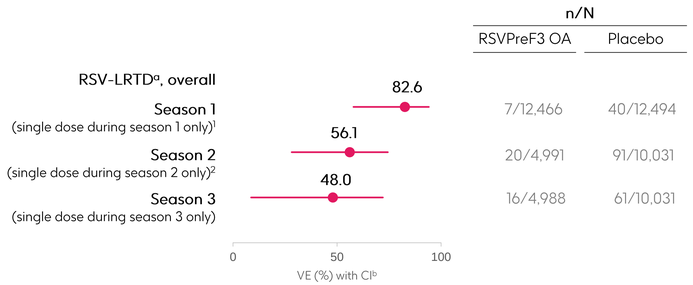


1. Papi A, et al. N Engl J Med. 2023;388:595-608; 2. Ison MG, et al. Clin Infect Dis. 2024;78:1732-44.

*Post-hoc analysis. [a]Case definition of RSV-LRTD: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours, with ≥1 RSV-positive swab detected by quantitative reverse transcriptase–polymerase chain reaction. [b]96.95% CI for season 1, 97.5% CI for season 1+2 and season 1+2+3. Dotted line: success criterion for confirmatory objectives (lower limit of CI >20%).

n, number of participants with ≥1 RSV-LRTD; N, number of participants in the modified exposed set.

VE against RSV-LRTD for each RSV season



1. Papi A, et al. N Engl J Med. 2023;388:595-608; 2. Ison MG, et al. Clin Infect Dis. 2024;78:1732-44.

[a]Case definition of respiratory syncytial virus-related lower respiratory tract disease (RSV-LRTD): ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours, with ≥1 RSV-positive swab detected by quantitative reverse transcriptase–polymerase chain reaction. [b]96.95% CI for season 1, 95% CI for season 2 and season 3.

VE, vaccine efficacy; CI, confidence interval; n, number of participants with ≥1 RSV-LRTD; N, number of participants in the modified exposed set (RSV season 1), dose 2-modified exposed set (season 2 and season 3).

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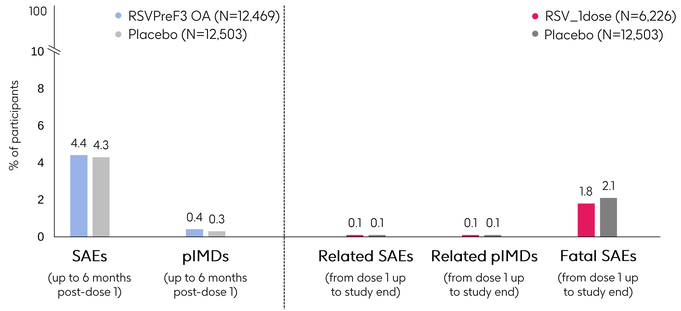
Supplementary material

Main page

The frequency of serious adverse events (SAEs) and potential immune-mediated diseases (pIMDs)



- No pattern of adverse events was identified.
- Reports of atrial fibrillation were below the expected incidence in the targeted population[1] and occurred in participants with high-risk profiles for onset of atrial fibrillation or in participants with pre-existing conditions.
- No cases of Guillain-Barré syndrome or acute disseminated encephalomyelitis were reported.

1. Morseth B, et al. Open Heart. 2021;8:e001624.

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Supplementary material

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9. Papi A, et al. N Engl J Med. 2023;388:595–608.
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Disclosures

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