Safety and Efficacy of Bivalent RSV Prefusion F Vaccine in Adults ≥ 60 Years of Age

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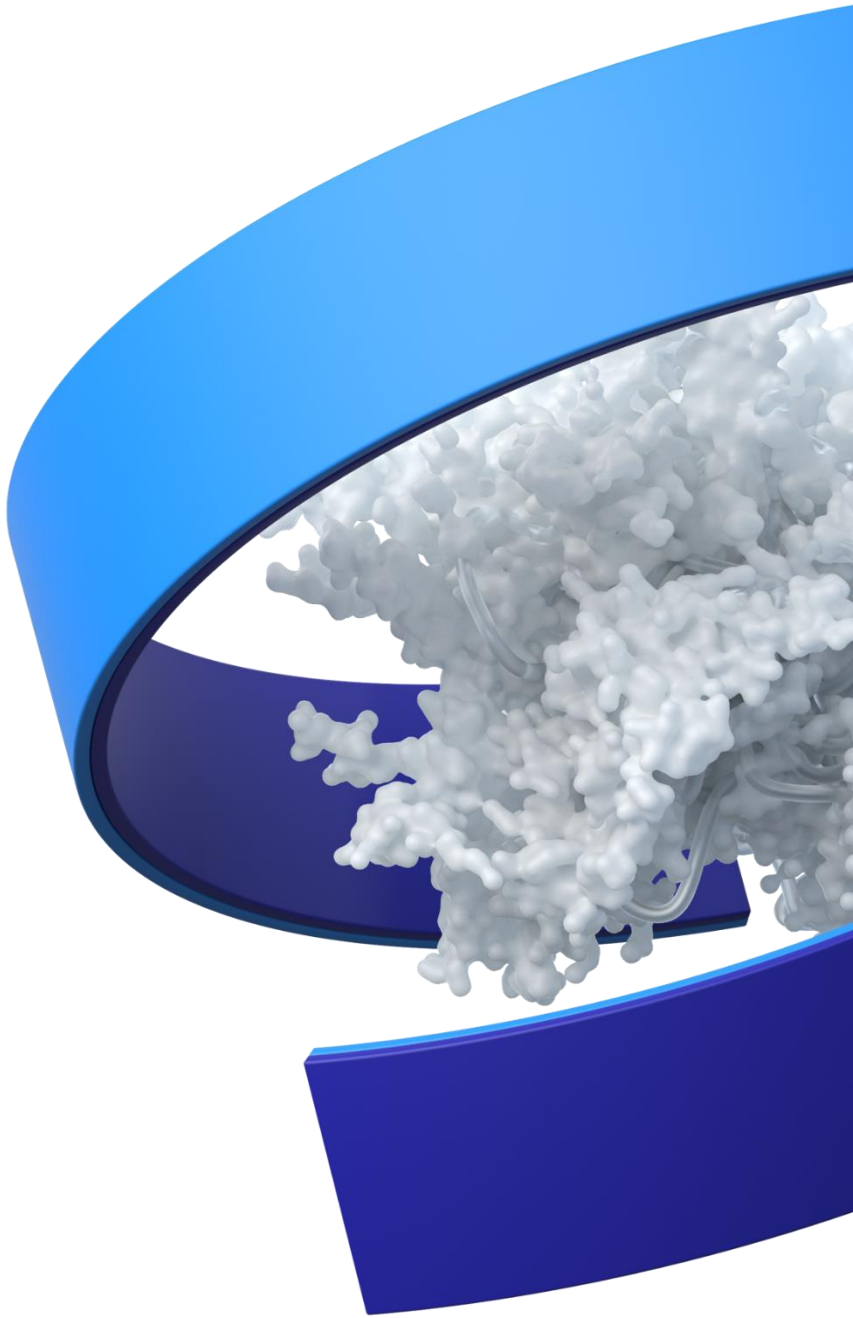
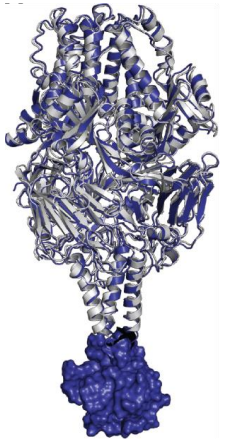


Pfizer's RSVpreF Vaccine Candidate Program

Vaccine

Bivalent stabilized prefusion F

- Sequence based on contemporary RSV A and RSV B strains
- Elicited high neutralizing titers for both RSV A and RSV B in Phase 1/2 studies[1,2,3]



Targeted Indications

Maternal

Immunize pregnant women to prevent RSV-associated lower respiratory tract illness (LRTI) in infants from birth through 6 months of age

Older adult

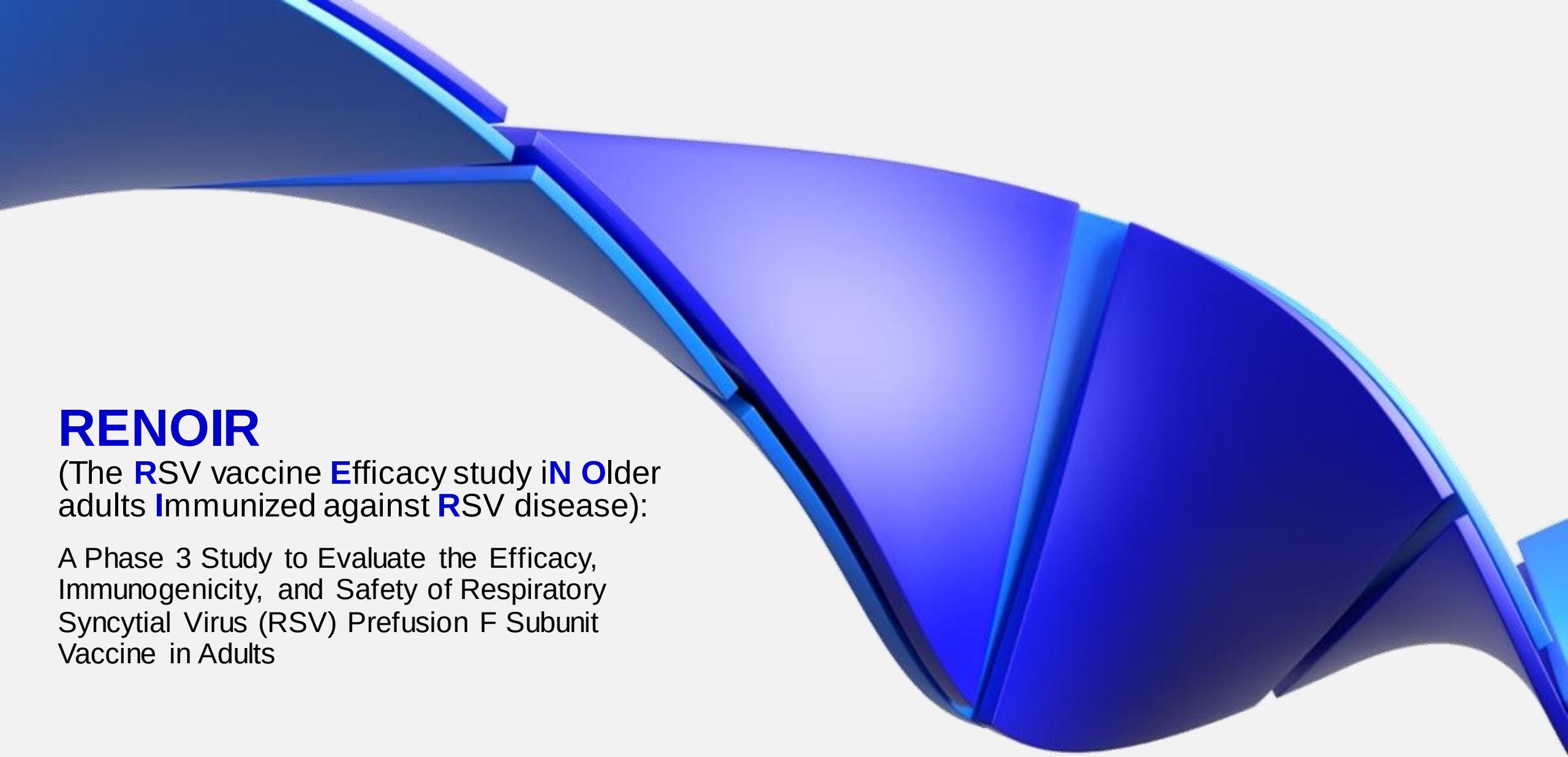
Active immunization to prevent RSV-associated LRTI in adults ≥ 60 years of age

[1]Falsey A., et al. J. Infect Dis 2022;225(12):2056-2066. [2]Walsh E., et al. J. Infect Dis 2022;225(8):1357-1366. [3]Baber J., et al. J. Infect Dis 2022 May 11;jiac189.

RSVpreF Older Adult Clinical Development Program

Study	Status	Brief Description	Age Group
C3671001[1] Phase 1/2	Completed	First-in-Human Dose Ranging +/- $Al(OH)_3$, +/- Influenza Vaccine Revaccination	18–85 years
C3671002[2] Phase 1/2	Completed	CpG/$Al(OH)_3$ Adjuvant Safety and Immunogenicity	65–85 years
WI257521[3] Phase 2a	Completed	Human Challenge Study	18–50 years
C3671014[4] Phase 3	Completed	Lot Consistency Study	18–49 years
C3671006[5] Phase 3	Ongoing	Concomitant Influenza Vaccine Study	≥ 65 years
C3671013[6] Phase 3	Ongoing	Pivotal Efficacy	≥ 60 years

1. A Study to Describe the Safety and Immunogenicity of a RSV Vaccine in Healthy Adults. NCT03529773; 2. A Study to Evaluatethe Safety and Immunogenicity of an Adjuvanted RSV Vaccine in Healthy Older Adults. NCT03572062; 3. Schmoele-Thoma B et al. Vaccine Efficacy in Adults in a Respiratory Syncytial Virus Challenge Study. N Engl J Med 2022; 386:2377-89. 4. Clinical Lot Consistency for RSVpreF in a Population of Healthy Adults 18 to ≤ 49 Years of Age. NCT05096208; 5. Safety and Immunogenicity of RSVpreF Coadministered with SIIV in Adults ≥ 65 Years of Age. NCT05301322; 6. Study to Evaluate the Efficacy, Immunogenicity, and Safety of RSVpreF in Adults (RENOIR). NCT05035212



RENOIR

(The **R**SV vaccine **E**fficacy study i**N** **O**lder adults **I**mmunized against **R**SV disease):

A Phase 3 Study to Evaluate the Efficacy, Immunogenicity, and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Subunit Vaccine in Adults

RENOIR Study Design I

240 study sites in 7 countries

Argentina   **Canada**

Finland   **Japan**

Netherlands   **South Africa**

U.S.

Targeted enrollment

Up to **40,000** participants

Adults **≥ 60 years**

Randomized 1:1 to receive RSVpreF 120 µg or placebo

Stratified by age group

60-69 years

70-79 years

≥ 80 years

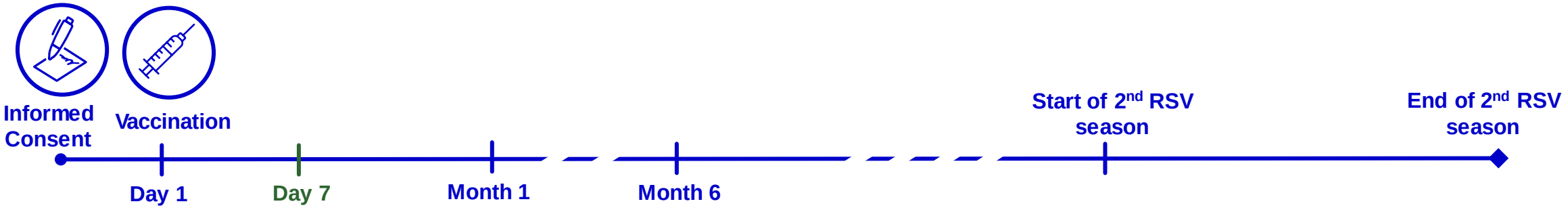
Key inclusion/exclusion criteria

☑ Healthy or with stable chronic conditions

☒ Immunocompromised persons with serious chronic disorders (e.g., metastatic cancer, ESRD)

Abbreviations: ESRD, end-stage renal disease

RENOIR Study Design II



Reactogenicity Subset
(N ~ 7,169)

Local reactions
Systemic events

All participants
(N ~ 34,284)

Unsolicited AEs

SAEs, NDCMCs

Weekly active surveillance for acute respiratory illness symptoms

Weekly active surveillance for acute respiratory illness symptoms

Immunogenicity Subset
(N ~ 1,050)

Blood draw pre-vaccination

Blood draw 1-month post-vaccination

Blood draw Start of 2nd RSV season

Abbreviations: AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event

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Key Study Definitions

Weekly active surveillance for ARI symptoms
Symptoms trigger nasal swab and possibly a visit

Acute Respiratory Illness (ARI)

1 or more of these symptoms (**new or worsened from baseline**), lasting more than 1 day

- Nasal discharge
- Nasal congestion
- Sore throat
- Cough
- Sputum production
- Wheezing
- Shortness of breath

RSV-ARI

Lower Respiratory Tract Illness (LRTI)

- Cough
- Sputum production
- Wheezing
- Shortness of breath
- Tachypnea

RSV-LRTI

ARI with ≥ 2 or ≥ 3 lower respiratory tract signs/symptoms (new or worsened)

Positive validated RT-PCR in central laboratory

Severe LRTI (sLRTI)

LRTI criteria plus at least 1 of the following:

- **Hospitalization** due to RSV-LRTI
- New/increased **oxygen supplementation**
- New/increased **mechanical ventilation** (including CPAP)

RSV-sLRTI

Phase 3 Study Objectives

Safety		• Describe the safety profile of RSVpreF Local reactions and systemic events within 7 days post-vaccination AEs through 1-month post-vaccination SAEs and NDCMCs throughout study
Efficacy	**Primary**	• Prevention of RSV-LRTI in the 1st RSV season VE of 1st episode RSV-LRTI involving ≥ 2 signs/symptoms in 1st RSV season VE of 1st episode RSV-LRTI involving ≥ 3 signs/symptoms in 1st RSV season
	Secondary	• Prevention of RSV-ARI in 1st season VE of 1st episode RSV-ARI in 1st season • Prevention of RSV-sLRTI in the 1st RSV season • Prevention of RSV-LRTI[1], RSV-ARI, RSV-sLRTI in 2nd RSV season • Prevention of RSV-LRTI[1], RSV-ARI, RSV-sLRTI across 2 RSV seasons

[1]Includes RSV-LRTI involving ≥ 2 signs/symptoms and RSV-LRTI involving ≥ 3 signs/symptoms

Abbreviations: AE, adverse event; ARI, acute respiratory illness; LRTI, lower respiratory tract illness; NDCMC, newly diagnosed chronic medical condition; RSV, respiratory syncytial virus; SAE, serious adverse event; sLRTI, severe lower respiratory tract illness; VE, vaccine efficacy

RENOIR – Statistical Considerations

- Preplanned interim analysis (IA), per protocol
- Agreement with regulatory agencies on licensure criteria
  - VE: lower bound of confidence interval >20%
  - Case definitions (RSV-LRTI, RSV-ARI, RSV-sLRTI) agreed upon with regulatory agencies
- Type I error adjustment for IA

Abbreviations: RSV, respiratory syncytial virus; ARI, acute respiratory illness; LRTI, lower respiratory tract illness; sLRTI, severe lower respiratory tract illness; VE, vaccine efficacy

RENOIR Results

Demographic Characteristics
(Safety Population)

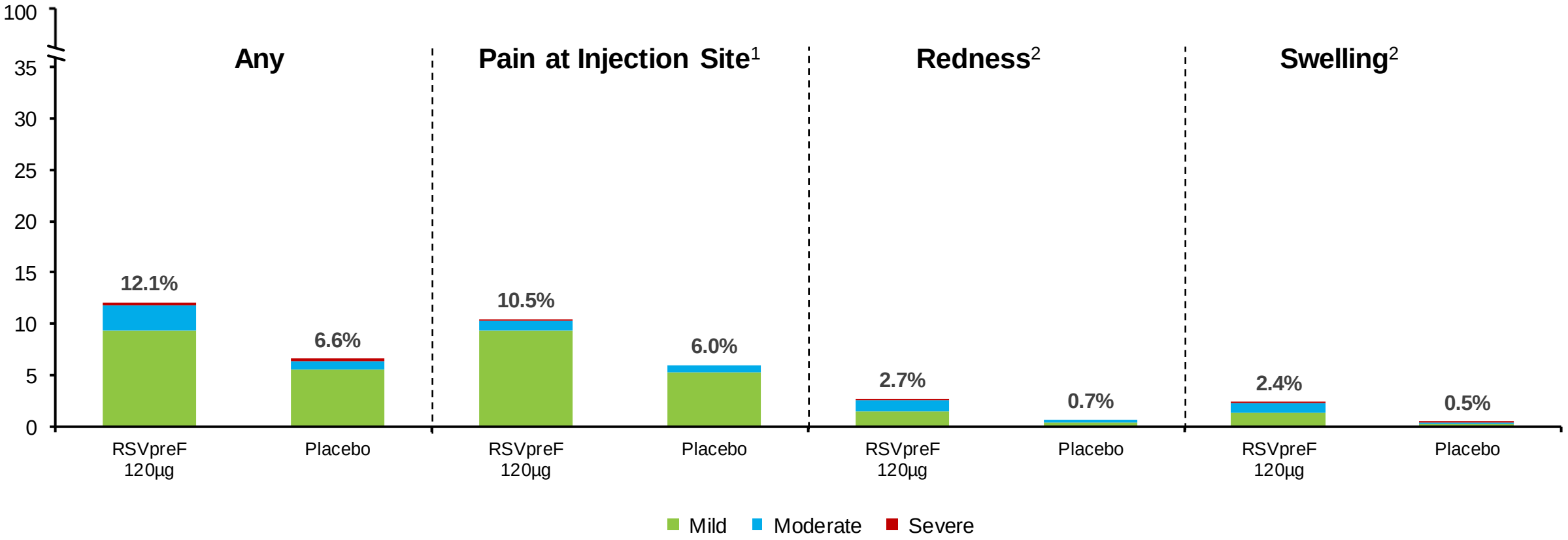
	RSVpreF 120 µg (N = 17,215); n (%)	Placebo (N = 17,069); n (%)	Total (N = 34,284); n (%)
Sex			
Male	8,800 (51.1)	8,601 (50.4)	17,401 (50.8)
Female	8,415 (48.9)	8,468 (49.6)	16,883 (49.2)
Race[1]			
White	13,475 (78.3)	13,360 (78.3)	26,835 (78.3)
Black or African American	2,206 (12.8)	2,207 (12.9)	4,413 (12.9)
Asian	1,352 (7.9)	1,333 (7.8)	2,685 (7.8)
American Indian or Alaska Native	44 (0.3)	36 (0.2)	80 (0.2)
Native Hawaiian or Other Pacific Islander	10 (<0.1)	15 (<0.1)	25 (<0.1)
Multiracial	44 (0.3)	36 (0.2)	80 (0.2)
Ethnicity			
Hispanic/Latino	6,384 (37.1)	6,260 (36.7)	12,644 (36.9)
Age at Vaccination			
<60 Years[2]	1 (<0.1)	0	1 (<0.1)
60-69 Years	10,756 (62.5)	10,680 (62.6)	21,436 (62.5)
70-79 Years	5,488 (31.9)	5,431 (31.8)	10,919 (31.8)
≥80 Years	970 (5.6)	958 (5.6)	1,928 (5.6)
Mean (SD)	68.3 (6.14)	68.3 (6.18)	68.3 (6.16)
Median (min, max)	67.0 (59, 95)	67.0 (60, 97)	67.0 (59, 97)

[1]Race was recorded as unknown in 0.2% in each group; race was not reported in 0.3% of each group
[2]One participant enrolled at age <60 years; because this participant received vaccine, the participant is included in the safety reporting

Baseline Characteristics – Prespecified Significant Conditions
(Safety Population)

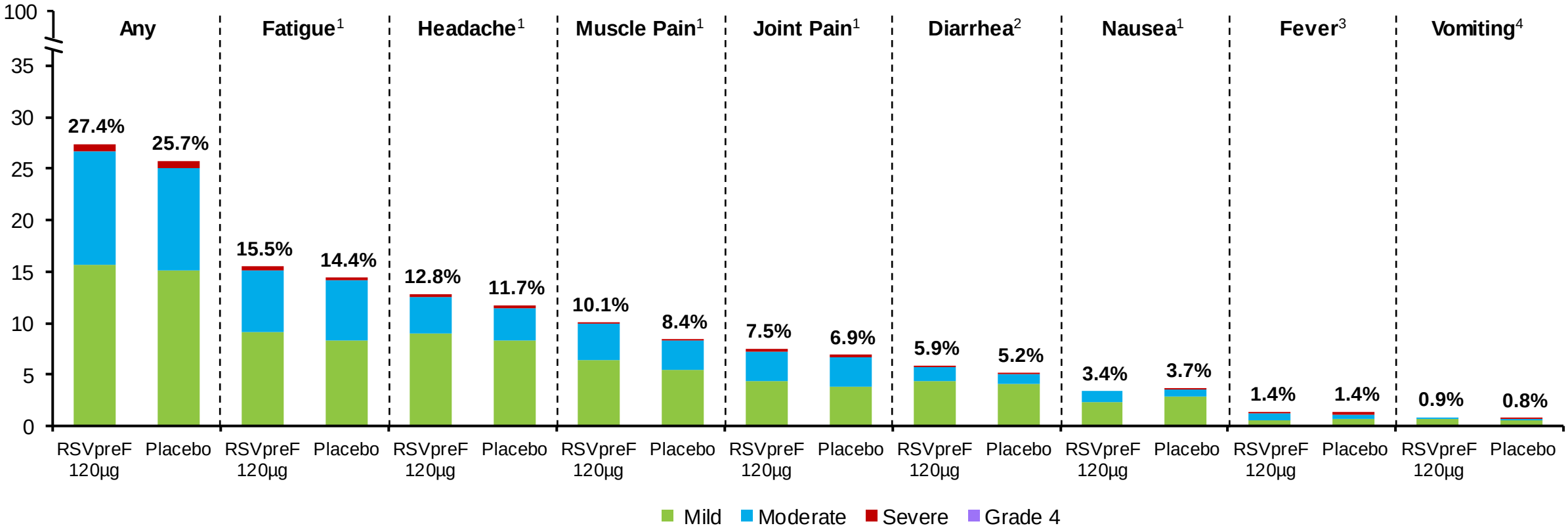
	RSVpreF 120 µg (N = 17,215) n (%)	Placebo (N = 17,069) n (%)	Total (N = 34,284) n (%)
Any prespecified significant condition	8,867 (51.5)	8,831 (51.7)	17,698 (51.6)
Heart disease	2,221 (12.9)	2,233 (13.1)	4,454 (13.0)
Lung disease	1,956 (11.4)	2,040 (12.0)	3,996 (11.7)
With ≥1 chronic cardiopulmonary condition	2,595 (15.1)	2,640 (15.5)	5,235 (15.3)
Asthma	1,541 (9.0)	1,508 (8.8)	3,049 (8.9)
Chronic obstructive pulmonary disease (COPD)	1,012 (5.9)	1,080 (6.3)	2,092 (6.1)
Congestive heart failure (CHF)	293 (1.7)	307 (1.8)	600 (1.8)
Diabetes	3,224 (18.7)	3,284 (19.2)	6,508 (19.0)
Liver disease	335 (1.9)	329 (1.9)	664 (1.9)
Renal disease	502 (2.9)	459 (2.7)	961 (2.8)
Current tobacco use	2,642 (15.3)	2,571 (15.1)	5,213 (15.2)

Local Reactions, by Maximum Severity, within 7 Days After Vaccination



[1]Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
[2]Severity definition: mild = >2-5 cm, moderate = >5-10 cm; severe = >10 cm
RSVpreF N = 3619-3621; placebo N = 3532-3539

Systemic Events, by Maximum Severity, Within 7 Days After Vaccination



[1]Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
[2]Severity definition: mild = 2-3 loose stools in 24h; moderate = 4-5 loose stools in 24h; severe = 6 or more loose stools in 24h
[3]Severity definition: mild 38.0°C-38.4 °C; moderate >38.4°C-38.9 °C; severe >38.9°C-40.0 °C; grade 4 >40.0 °C
[4]Severity definition: mild = 1-2 time(s) in 24h; moderate = >2 times in 24h; severe = requires intravenous hydration
RSVpreF N = 3619-3621: Placebo N = 3532-3539

Adverse Events, by Category, from Vaccination through 1-Month Follow Up Visit and through Data Cutoff (14Jul2022) — Safety Population

Adverse Event Category	RSVpreF 120 µg (N = 17,215) n (%)	(95% CI)	Placebo (N = 17,069) n (%)	(95% CI)
From Vaccination through 1-Month Follow-Up Visit				
Any Event	1,544 (9.0)	(8.5, 9.4)	1,453 (8.5)	(8.1, 8.9)
Related	239 (1.4)	(1.2, 1.6)	163 (1.0)	(0.8, 1.1)
Immediate AE[1]	37 (0.2)	(0.2, 0.3)	31 (0.2)	(0.1, 0.3)
Severe	65 (0.4)	(0.3, 0.5)	51 (0.3)	(0.2, 0.4)
Life-threatening	24 (0.1)	(0.1, 0.2)	19 (0.1)	(0.1, 0.2)
From Vaccination through 14Jul2022				
NDCMC	301 (1.7)	(1.6, 2.0)	313 (1.8)	(1.6, 2.0)
SAE	396 (2.3)	(2.1, 2.5)	387 (2.3)	(2.0, 2.5)
Related SAE	3 (<0.1)	(0.0, 0.1)	0	(0.0, 0.0)
AE leading to withdrawal	10 (<0.1)	(0.0, 0.1)	6 (<0.1)	(0.0, 0.1)
AE leading to death	52 (0.3)	(0.2, 0.4)	49 (0.3)	(0.2, 0.4)

Note: Any reactogenicity reported as adverse events (from either reactogenicity subset or non-reactogenicity subset) during the specified time period are included in this table
[1]Immediate AE refers to an AE reported in the 30-minute post-vaccination observation period

Abbreviations: AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event

Serious Adverse Events Assessed as Related by the Investigator
n = 3 (<0.1%)

- Hypersensitivity
  - Delayed allergic reaction
  - Determined as not anaphylaxis
- Miller Fisher Syndrome
  - Retrospective diagnosis
  - Anti-GQ1b IgG negative; spinal tap, nerve conduction studies not performed
  - Brighton criteria Level 4
- Guillain-Barre Syndrome
  - Non-ST elevation myocardial infarction
  - Nerve conduction study – acute demyelinating polyneuritis of lower extremities
  - Brighton criteria Level 1

Efficacy

RSVpreF was highly efficacious against RSV-LRTI during the first season

Both primary efficacy endpoints met licensure criteria

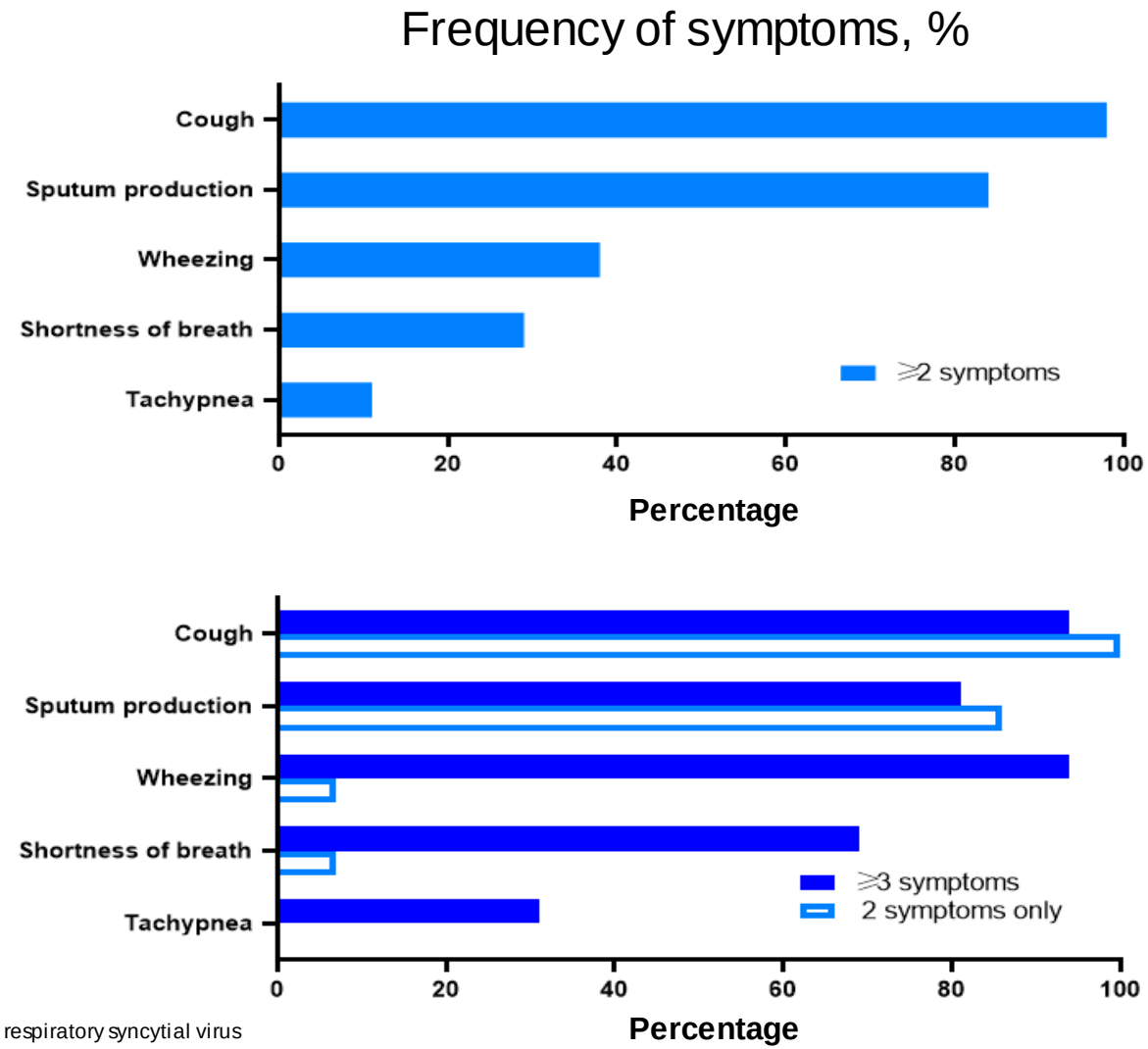
Total cases ≥ 2 RSV-LRTI	Case split RSVpreF/Placebo	VE	96.66% CI[1]
44	**11/33**	**66.7%**	**(28.8%, 85.8%)**

Total cases ≥ 3 RSV-LRTI	Case split RSVpreF/Placebo	VE	96.66% CI[1]
16	**2/14**	**85.7%**	**(32.0%, 98.7%)**

[1]CI obtained using the conditional exact test based on the binomial distribution of P, adjusted by Pocock error spending for interim analysis (alpha = 3.34%)

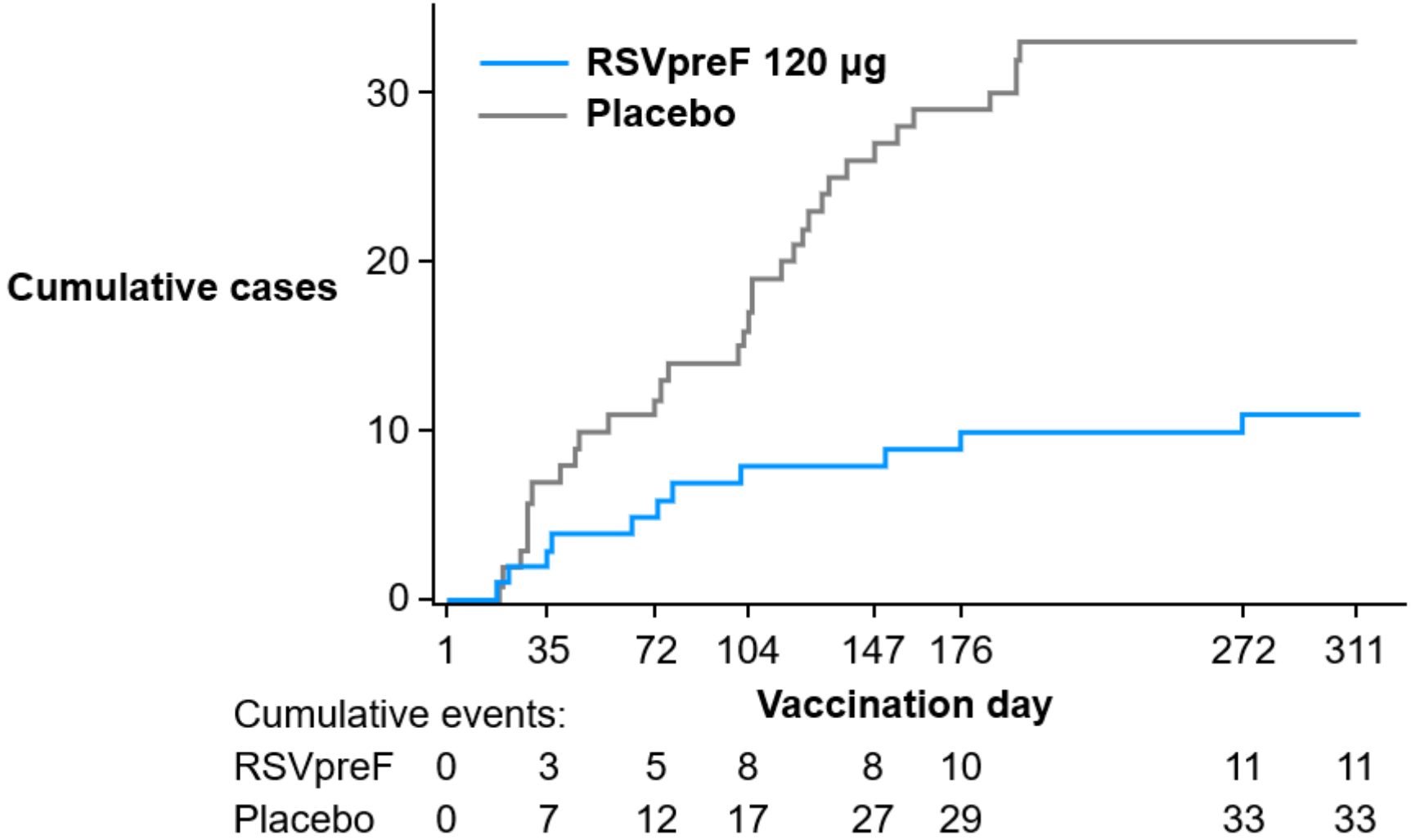
Abbreviations: CI, confidence interval; RSV-LRTI, lower respiratory tract illness due to respiratory syncytial virus; VE, vaccine efficacy

RSV-LRTI with ≥ 3 signs/symptoms associated with more severe illness



Abbreviations: RSV-LRTI, lower respiratory tract illness due to respiratory syncytial virus

RSVpreF efficacy against RSV-LRTI with ≥ 2 symptoms



Mean active surveillance: 7 months

Abbreviations: RSV-LRTI, lower respiratory tract illness due to respiratory syncytial virus

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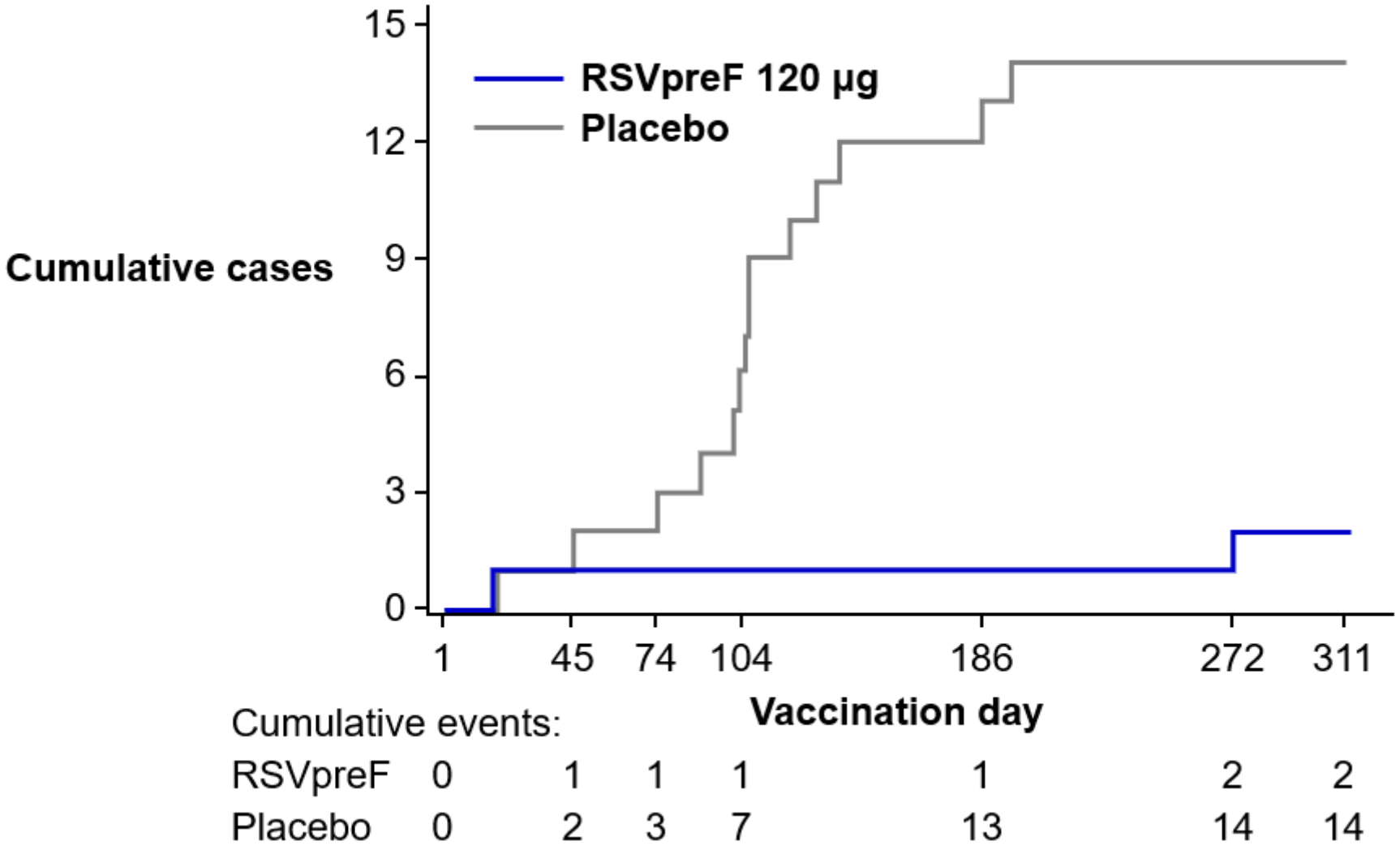
RSVpreF efficacy against RSV-LRTI with **≥ 3 symptoms**



Mean active surveillance: 7 months

Abbreviations: RSV-LRTI, lower respiratory tract illness due to respiratory syncytial virus

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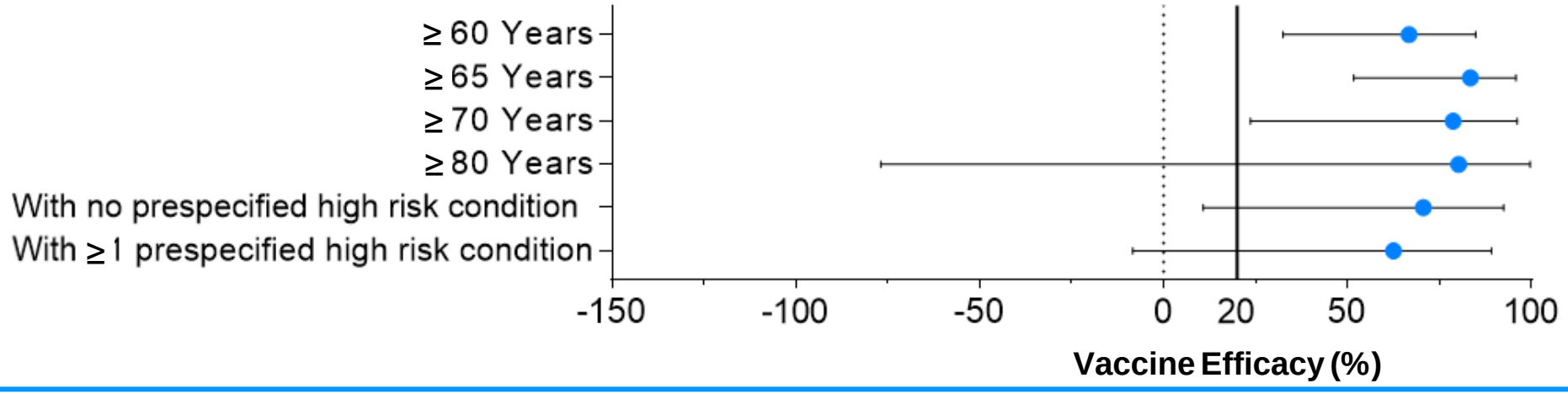
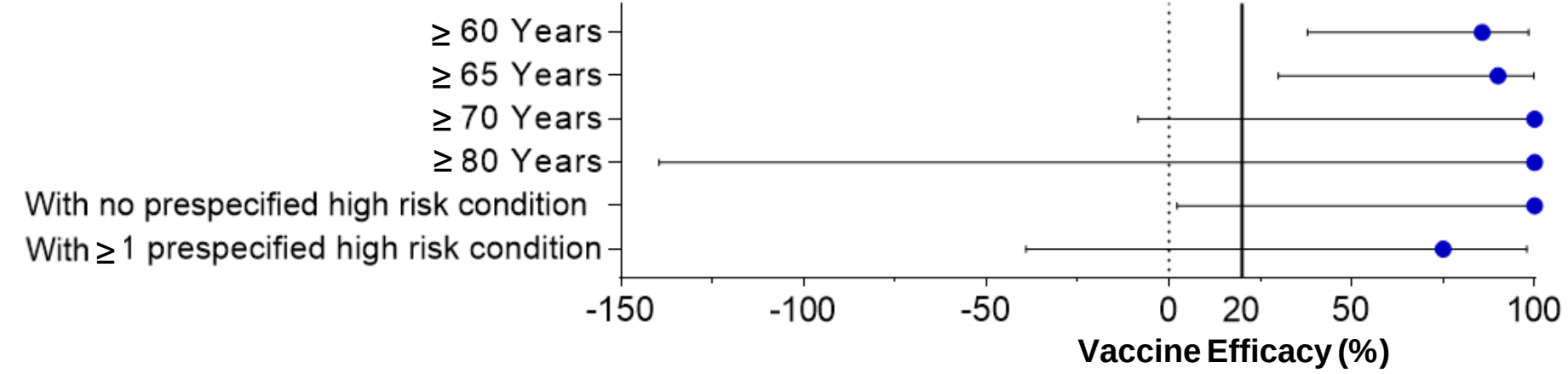
Consistent efficacy was observed across population subgroup analyses

≥ 2 Symptoms



	Case Split (RSVpreF/Placebo)	VE
≥ 60 Years	11/33	66.7%
≥ 65 Years	4/24	83.4%
≥ 70 Years	3/14	78.7%
≥ 80 Years	1/5	80.2%
With no prespecified high risk condition	5/17	70.6%
With ≥ 1 prespecified high risk condition	6/16	62.5%

≥ 3 Symptoms

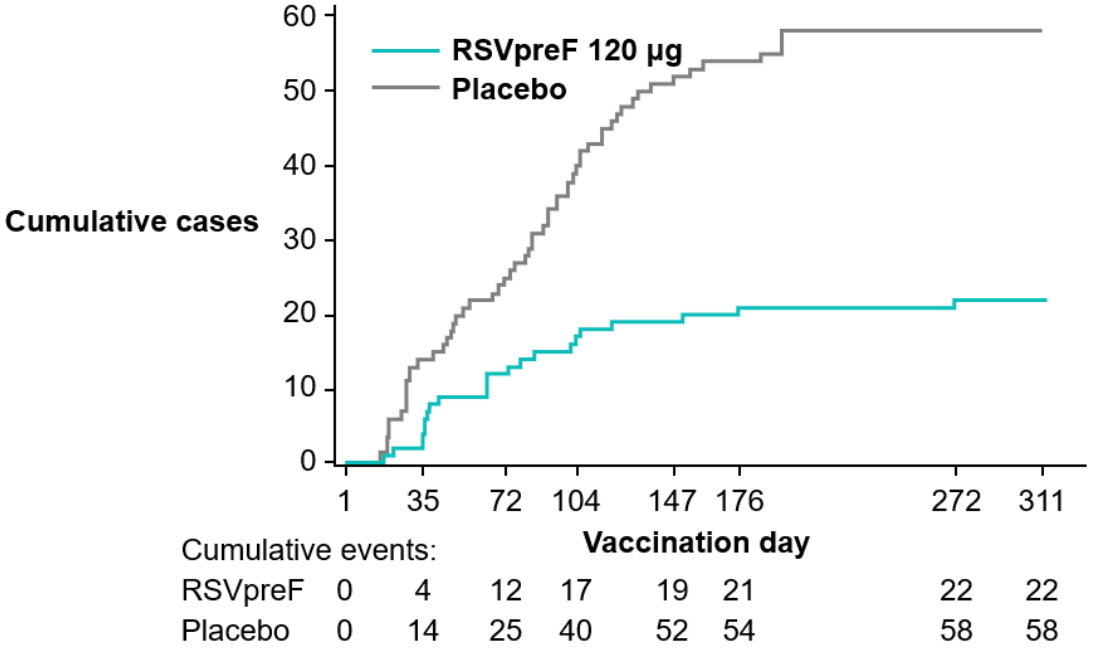


	Case Split (RSVpreF/Placebo)	VE
≥ 60 Years	2/14	85.7%
≥ 65 Years	1/10	90.0%
≥ 70 Years	0/5	100%
≥ 80 Years	0/3	100%
With no prespecified high risk condition	0/6	100%
With ≥ 1 prespecified high risk condition	2/8	75.0%

Note: Horizontal bars depict 95% confidence interval
Abbreviations: VE, vaccine efficacy

RSVpreF efficacy against RSV-ARI

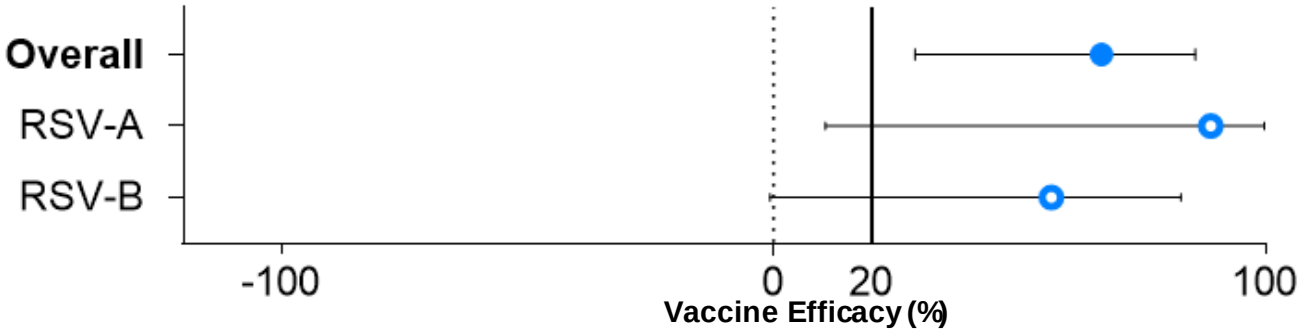
Total cases RSV-ARI	Case split RSVpreF/Placebo	VE	95% CI
80	22/58	62.1%	(37.1%, 77.9%)



Abbreviations: CI, confidence interval; RSV-ARI, acute respiratory illness due to respiratory syncytial virus; VE, vaccine efficacy.

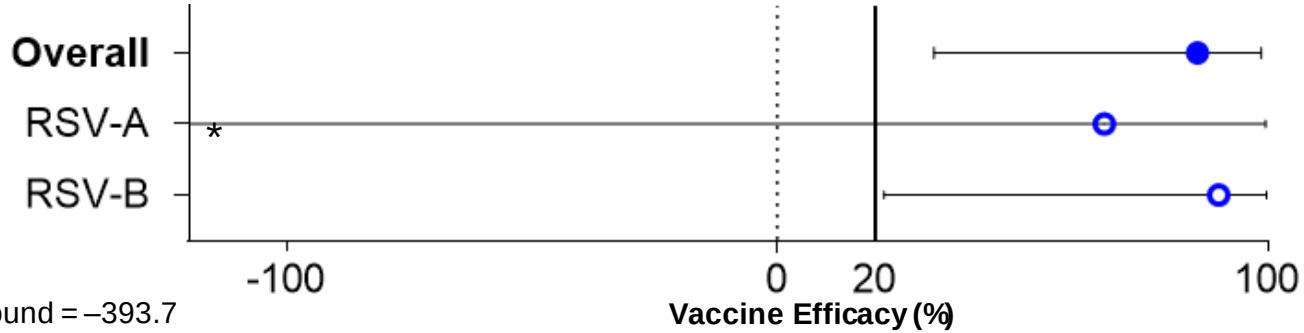
Consistent efficacy was observed across RSV subgroup A and B

RSV-LRTI ≥ 2 Symptoms



	Case Split (RSVpreF/Placebo)	VE
Overall		
RSV-A	1/9	88.9%
RSV-B	10/23	56.5%

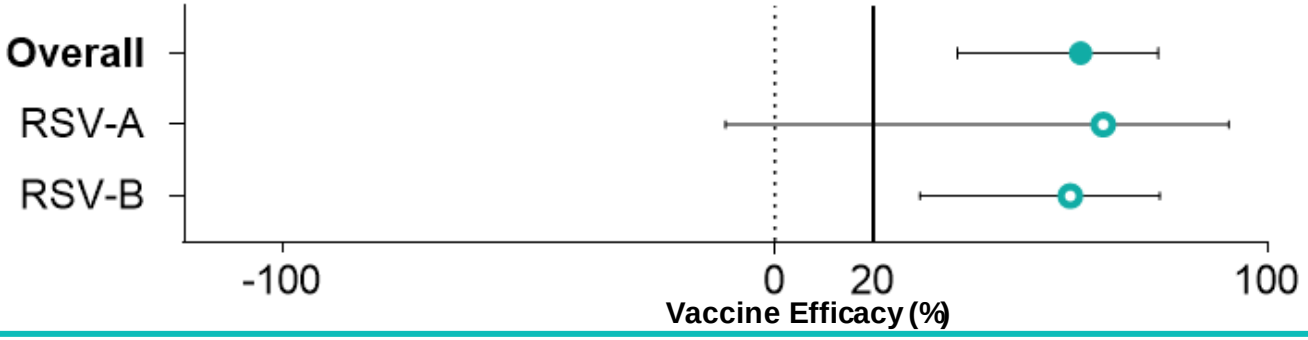
RSV-LRTI ≥ 3 Symptoms



	Case Split (RSVpreF/Placebo)	VE
Overall		
RSV-A	1/3	66.7%
RSV-B	1/10	90.0%

* Lower bound = –393.7

RSV-ARI



	Case Split (RSVpreF/Placebo)	VE
Overall		
RSV-A	4/12	66.7%
RSV-B	18/45	60.1%

Notes: (1) 95% CI for RSV-ARI and 96.66% CI for RSV-LRTI; (2) One case in placebo group was based on local test without RSV subgroup
Abbreviations: ARI, acute respiratory illness; LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus; VE, vaccine efficacy.

Phase 3 Efficacy Interim Analysis

Safety Conclusions

- RSVpreF was safe and well tolerated
- Local and systemic events were mostly mild to moderate and short lived
- AE profile did not suggest any safety concerns for RSVpreF vaccination in adults 60 years of age and older

Efficacy Conclusions

- RSVpreF was highly efficacious in reducing RSV-associated LRTI in adults 60 years and older
- RSVpreF was efficacious in reducing RSV-associated ARI in adults 60 years and older

Acknowledgments

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- The clinical trial participants
- Sites, investigators, CRO, our partners, and their staff