Efficacy and Safety of Bivalent Respiratory Syncytial Virus (RSVpreF) Vaccine in Older Adults

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Disclosures

- Edward E. Walsh reports grants from Merck, Pfizer, and Janssen; and has served as an unpaid consultant to Novavax, Merck, GlaxoSmithKline, and Janssen.
- Fernando Polack holds stock in iTrials SA, and is a consultant for Janssen, Merck, and Novovax.
- Ann F. Falsey reports grants from Merck, Pfizer, BioFire Diagnostics, Janssen, and CyanVac; serves on a Data and Safety Monitoring Board for Novavax; and is a consultant for GSK, Icosavax and Arrowhead Pharmaceuticals.
- Gonzalo Pérez Marc has conducted clinical trials for Pfizer, Boehringer Ingelheim, Janssen, Medicago, and Merck.
- Agnieszka M. Zareba, Qin Jiang, Katherine Schneider, David Cooper, Maria Maddalena Lino, Annaliesa S. Anderson, Kena A. Swanson, Alejandra Gurtman, William C. Gruber, and Beate Schmoele-Thoma are Pfizer employees and may hold stock or stock options.
- Kathrin U. Jansen was a Pfizer employee at the time of the study and may hold stock or stock options.

RSV is a hidden annual epidemic in older adults

True burden in older adults is **underestimated**
because testing is not routinely done and when performed is unreliable

Annual burden

US adults 65 years and older

5.5% attack rate resulting in
2.6 million cases each year

177,000
hospitalizations

14,000
deaths

Important cause of morbidity and mortality that rivals influenza

- **~25–50% of that attributed to influenza A(H3N2)**
- **Similar to rates observed in some years for A(H1N1) and influenza B**

Who is at risk?

Older adults

+

Adults with selected chronic conditions (e.g., heart or lung disease)

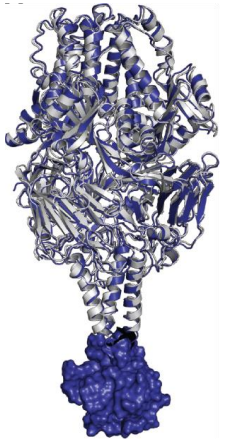
Sources: McLaughlin J et al. Open Forum Infect Dis 2022;9:ofac300; National Foundation for Infectious Diseases. Respiratory Syncytial Virus in Older Adults: A Hidden Annual Epidemic, Sep 2016. www.nfid.org/publications/reports/rsv-report.pdf; Falsey A et al. N Engl J Med 2005;352:1749–1759; Matias G et al. BMC Public Health 2017;17:271; Fleming DM et al. BMC Infect Dis 2015;15:433; Matias G et al. Influenza Other Respir Viruses 2014;8:507–515; Thompson WW et al. JAMA 2003;289:179–186.
Abbreviations: RSV, respiratory syncytial virus.

RSVpreF vaccine

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[1-3]



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

Sources: [1]Falsey A et al. J Infect Dis 2022;225:2056–2066; [2]Walsh E et al. J Infect Dis 2022;225:1357–1366; [3]Baber J et al. J Infect Dis 2022 May 11;jiac189.
Abbreviations: RSV, respiratory syncytial virus.

Study design

240 study sites in 7 countries

Argentina
Canada
Finland
Japan
Netherlands
South Africa
United States

Targeted enrollment

Up to **40,000** participants
Adults **≥60 years old**

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)

First participants enrolled: August 31, 2021 (Northern Hemisphere) and November 23, 2021 (Southern Hemisphere)

Abbreviations: ESRD, end-stage renal disease; LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus.

Study schedule

Vaccination

7 days post-vaccination

Pre-planned efficacy interim analysis

Analysis after 1 season

Reactogenicity subset (N ~ 6450)

Local reactions
Systemic events

Based on case accrual

Primary efficacy Efficacy **of RSVpreF in preventing RSV-LRTI with ≥2 or ≥3 symptoms/signs in the first RSV season**

All participants: Weekly active surveillance for acute respiratory illness (ARI) symptoms: Symptoms **TRIGGER** nasal swab and possibly a visit

RSV-ARI:
≥1 of these symptoms for >1 day

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

RSV-LRTI:
≥2 or ≥3 of these symptoms within 7 days of ARI onset

Cough	Wheezing	Sputum production	Shortness of breath	Tachypnea

+ **Positive validated RT-PCR**

Abbreviations: ARI, acute respiratory illness; LTRI, lower respiratory tract infection; RSV, respiratory syncytial virus; RT-PCR, reverse transcription-polymerase chain reaction.

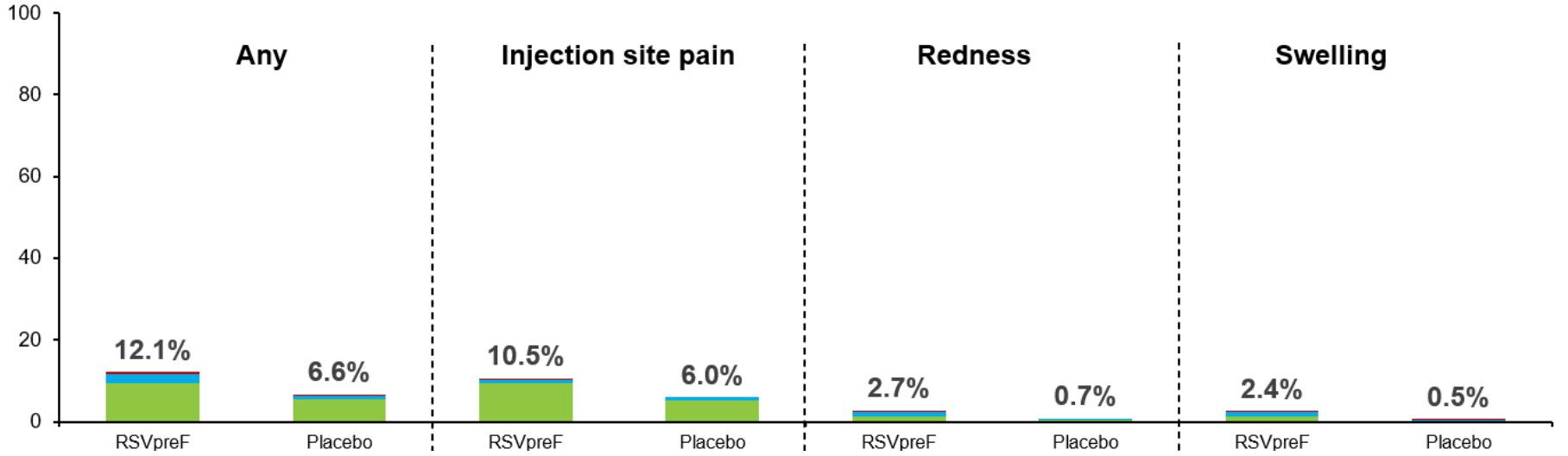
Demographic and baseline characteristics

	RSVpreF (N=17,215)	Placebo (N=17,069)
Male, n (%)	8800 (51.1)	8601 (50.4)
Race, n (%)		
White	13,475 (78.3)	13,360 (78.3)
Black or African American	2206 (12.8)	2207 (12.9)
Asian	1352 (7.9)	1333 (7.8)
Hispanic/Latino ethnicity, n (%)	6384 (37.1)	6260 (36.7)
Age at vaccination, n (%)		
60−69 years	10,756 (62.5)	10,680 (62.6)
70−79 years	5488 (31.9)	5431 (31.8)
≥80 years	970 (5.6)	958 (5.6)
Mean (SD) years	68.3 (6.14)	68.3 (6.18)
Prespecified high-risk condition, n (%)		
≥1 Chronic cardiopulmonary condition	2595 (15.1)	2640 (15.5)
Asthma	1541 (9.0)	1508 (8.8)
Chronic obstructive pulmonary disease	1012 (5.9)	1080 (6.3)
Congestive heart failure	293 (1.7)	307 (1.8)
Diabetes	3224 (18.7)	3284 (19.2)
Heart disease	2221 (12.9)	2233 (13.1)
Without any high-risk condition, n (%)	8348 (48.5)	8238 (48.3)

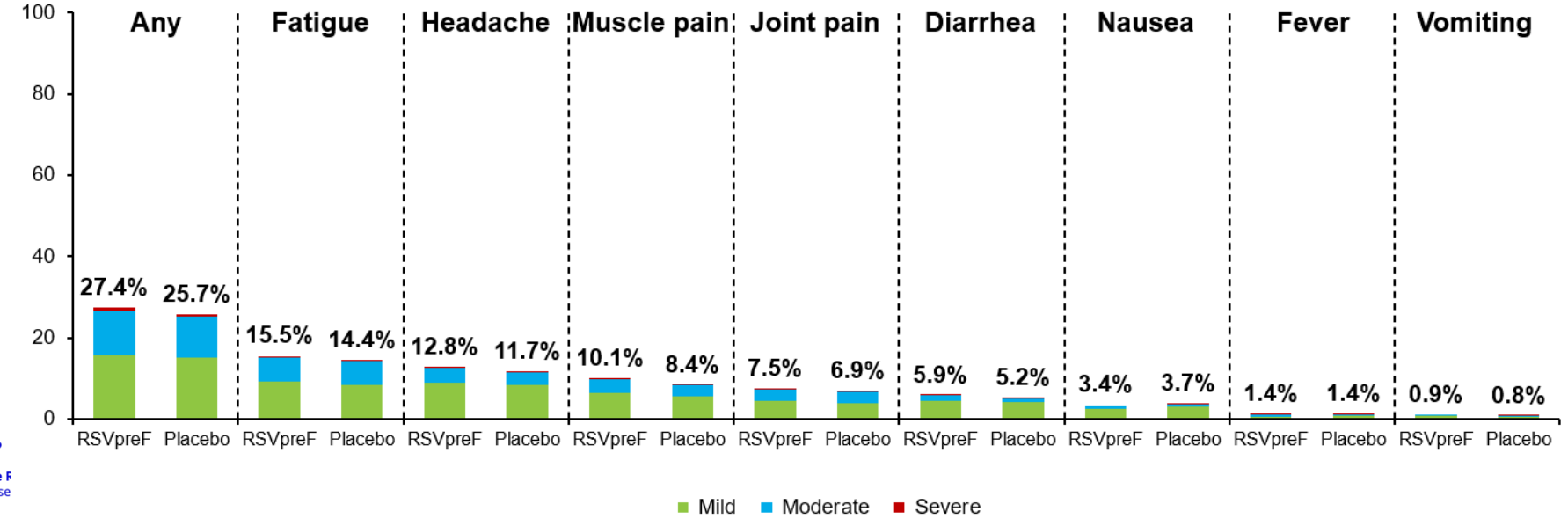
RSVpreF was well tolerated

Percentage of participants with reactogenicity events by maximum severity within 7 days after vaccination

Local reactions



Systemic events

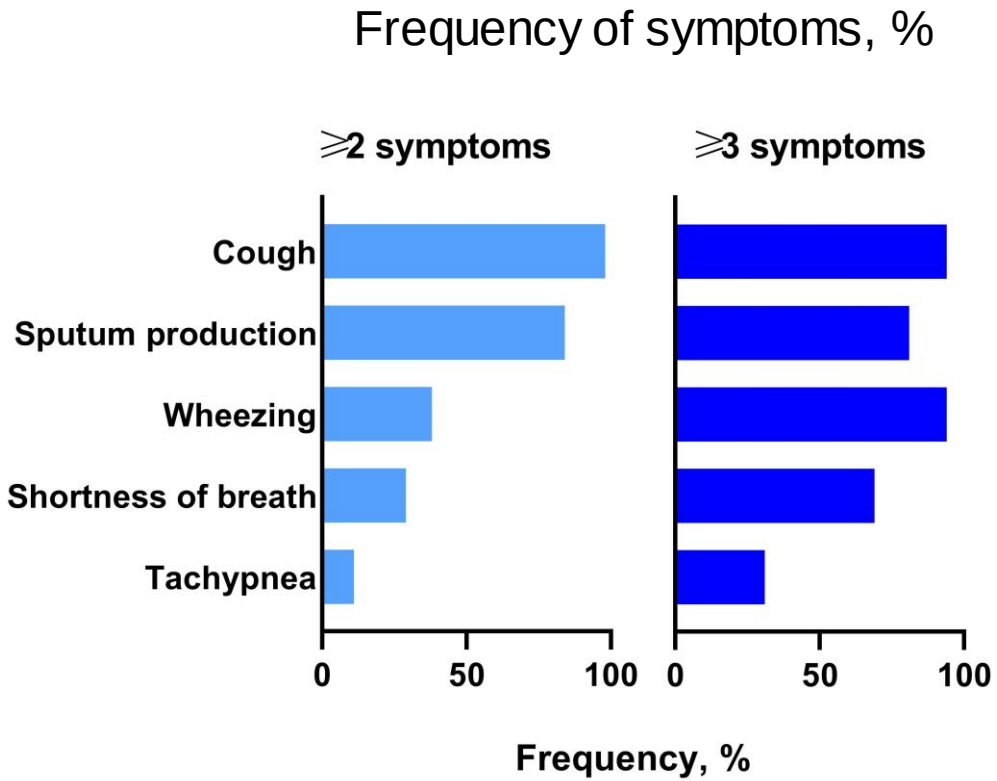


RSVpreF was highly efficacious against RSV-LRTI during the first season

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)

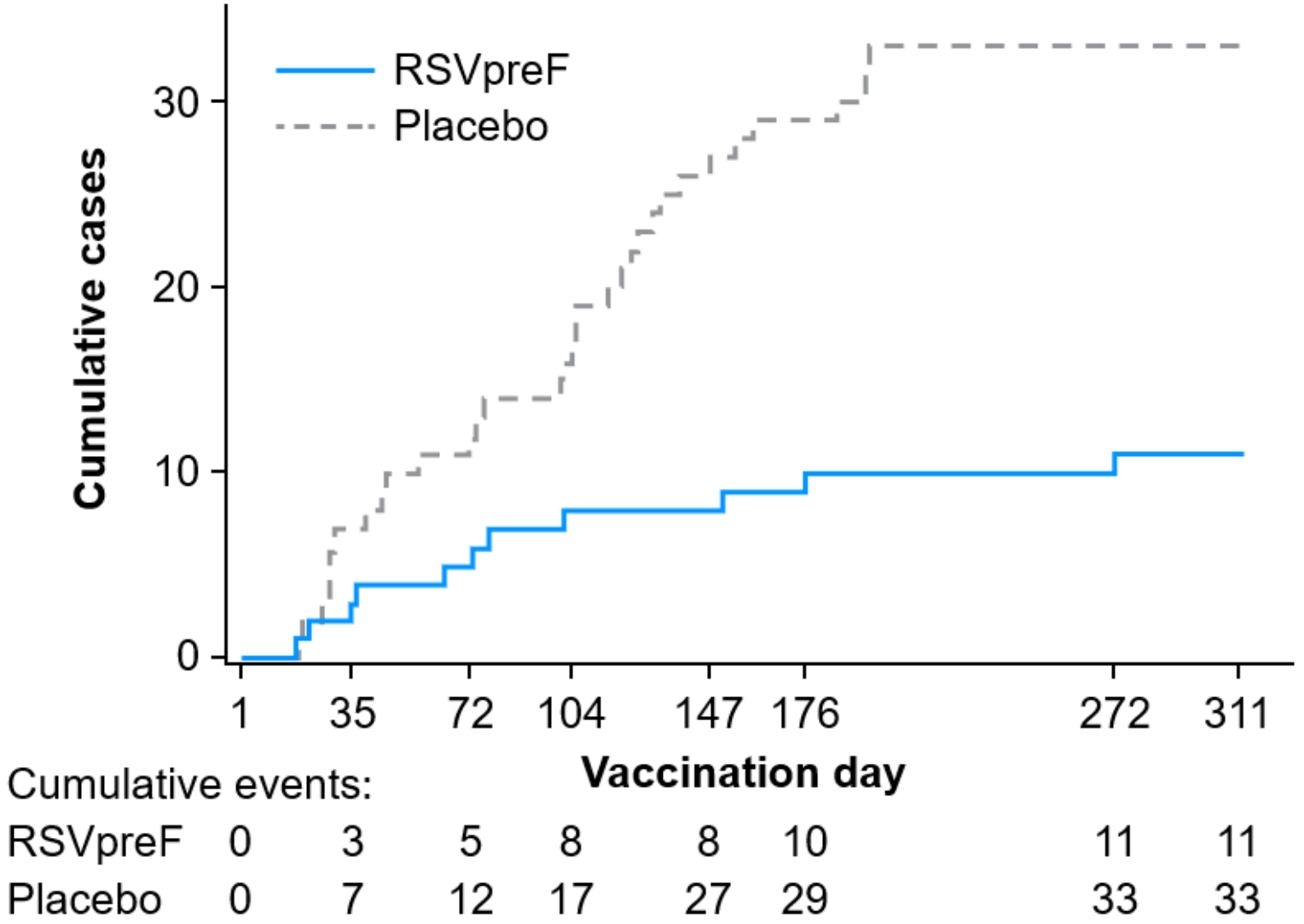
[1]CI obtained using the conditional exact test based on the binomial distribution of P, adjusted by Pocock error spending for interim analysis (alpha=3.34%)



- **Both primary efficacy endpoints were met**

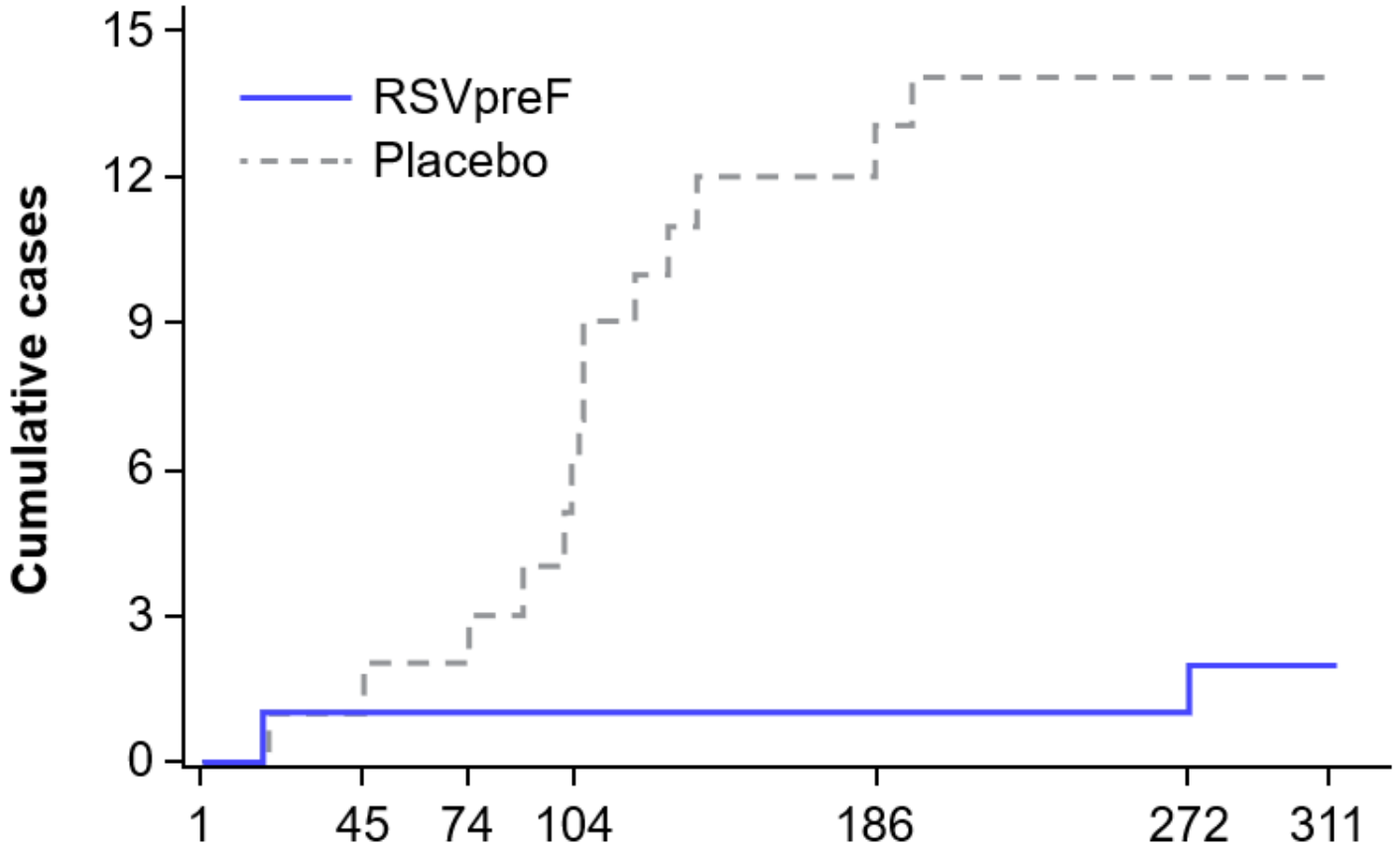
Abbreviations: LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus; RT-PCR, reverse transcription-polymerase chain reaction; VE, vaccine efficacy.

RSVpreF efficacy against RSV-LRTI with ≥2 symptoms



Mean active surveillance:
7 pts-months

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



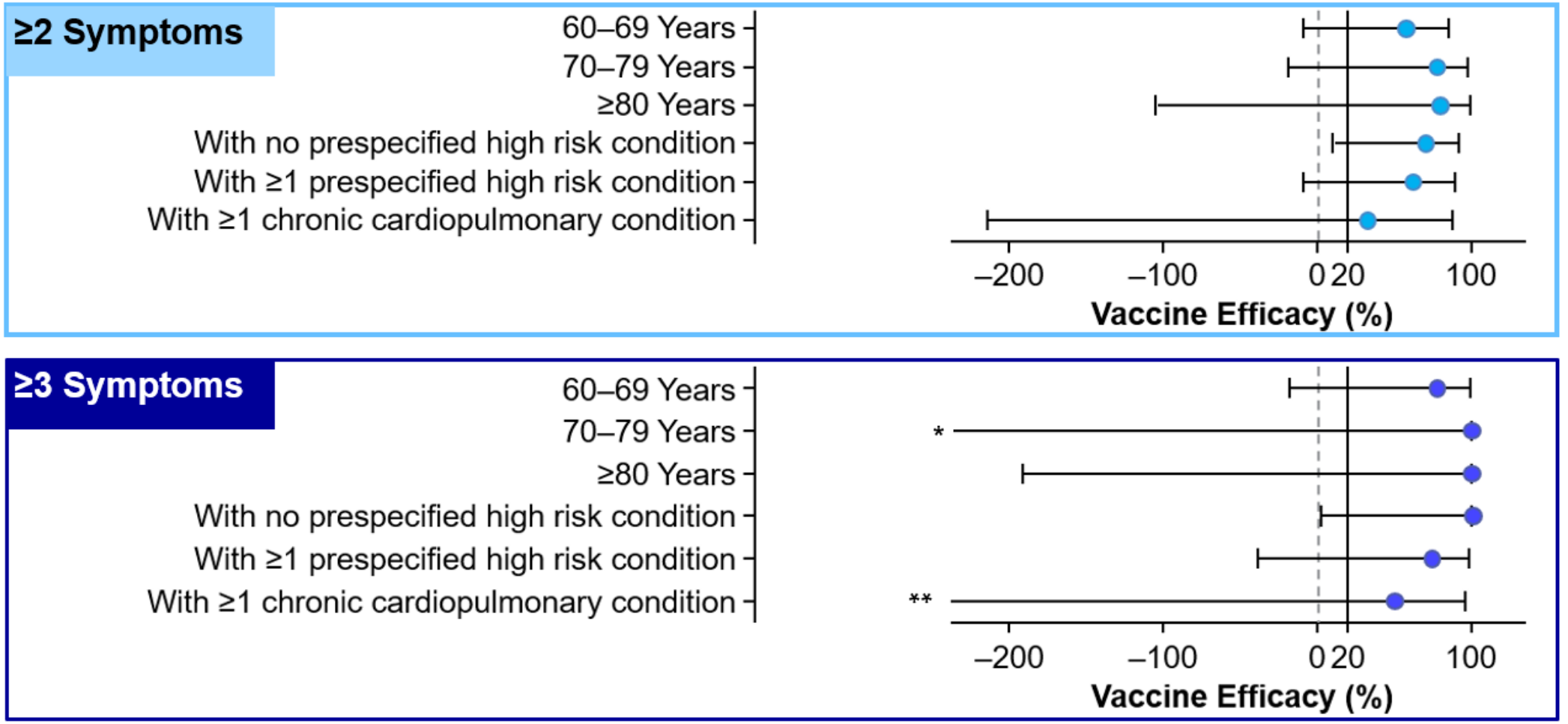
Cumulative events:

RSVpreF	0	1	1	1	1	2	2
Placebo	0	2	3	7	13	14	14

Mean active surveillance:
7 pts-months

Consistent efficacy was observed across subgroup analyses

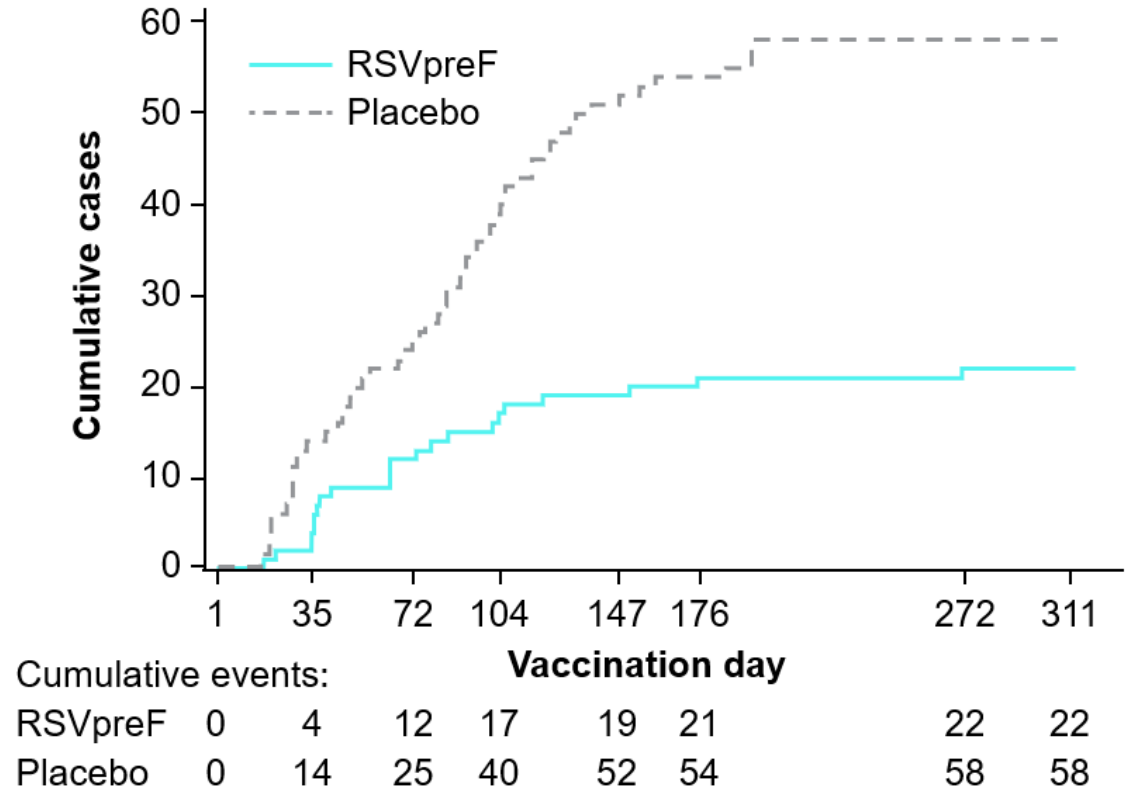
Demographic baseline characteristic



* Lower bound = –573.8.
** Lower bound = –302.1.

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: ARI, acute respiratory illness; RSV, respiratory syncytial virus; VE, vaccine efficacy.

Interim analysis conclusions from phase 3 efficacy in adults ≥60 years of age

Safety

- RSVpreF was safe and well tolerated
- Local and systemic events were mostly mild to moderate and short lived

Efficacy

- RSVpreF was highly efficacious in reducing RSV-associated LRTI and ARI through the interim analysis
- Efficacy through Season 2 is planned to assess duration of protection

Abbreviations: ARI, acute respiratory illness; LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus.

Acknowledgments

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

Backup slides

Vaccine efficacy of RSVpreF against first episode of RSV-LRTI with ≥2 or ≥3 symptoms, by RSV subgroup

	Total cases ≥2 RSV-LRTI	Case split RSVpreF/Placebo	VE	96.66% CI
Overall[1]	44	11/33	66.7%	(28.8, 85.8)
Subgroup A	10	1/9	88.9%	(10.6, 99.8)
Subgroup B	33	10/23	56.5%	(−0.7, 82.8)

	Total cases ≥3 RSV-LRTI	Case split RSVpreF/Placebo	VE	96.66% CI
Overall[1]	16	2/14	85.7%	(32.0, 98.7)
Subgroup A	4	1/3	66.7%	(−393.7, 99.6)
Subgroup B	11	1/10	90.0%	(21.8, 99.8)

[1]One positive RSV PCR test from a local laboratory without subgroup information is included in the count of RSV-ARI (but not included in any subgroup rows), as there was no swab within 7 days of symptom onset for central laboratory testing available.

Abbreviations: LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus; VE, vaccine efficacy.