Clinical Infectious Diseases

MAJOR ARTICLE

Bivalent RSVpreF Vaccine in Adults 18 to <60 Years Old With High-Risk Conditions

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Background. Older individuals and adults with certain chronic or immunocompromising health conditions are at increased risk of severe respiratory syncytial virus (RSV) disease.

Methods. In this phase 3 randomized trial of RSVpreF safety and immunogenicity in 18–59-year-olds at high risk of severe RSV disease, participants were randomized 2:1 to 1 RSVpreF (120 μg) or placebo dose. Primary safety endpoints included reactogenicity events and adverse events (AEs) through 7 days and 1 month after vaccination, respectively, and serious AEs (SAEs) and newly diagnosed chronic medical conditions (NDCMCs) throughout the study. In primary analyses, immunogenicity elicited 1 month after RSVpreF was bridged to a randomly selected subset of ≥60-year-olds receiving RSVpreF from the immunogenicity subset in the pivotal phase 3 RENOIR trial, which demonstrated RSVpreF efficacy. Noninferiority was declared if 95% confidence interval (CI) lower bounds were >.667 (neutralizing titer adjusted geometric mean ratios) and >−10% (seroresponse rate differences) for RSV-A and RSV-B.

Results. Overall, 678 participants received RSVpreF (n = 453) or placebo (n = 225). Most reactogenicity events were mild/moderate; severe events occurred in ≤2.0% of participants overall. AE frequencies were similar in RSVpreF (7.1%) and placebo recipients (7.6%). No vaccine-related SAEs or NDCMCs were reported. One month after RSVpreF administration, noninferiority criteria were met in 18–59-year-olds versus ≥60-year-olds for RSV-A and RSV-B neutralizing titers and seroresponse rates.

Conclusions. RSVpreF was well tolerated with no safety concerns and demonstrated immunobridging to efficacy in 18–59-year-olds at high risk of severe RSV disease versus ≥60-year-olds in whom efficacy was previously demonstrated, supporting use of RSVpreF to prevent RSV-associated disease in this population. NCT05842967.

Keywords. RSV; RSVpreF; vaccine; immunogenicity; safety.

Respiratory syncytial virus (RSV) is an important cause of severe respiratory disease in infants, older adults, and those with health conditions that increase the risk of severe RSV illness [1, 2]. These risk factors in adults are similar to those for severe influenza and include older age, chronic cardiac and pulmonary disease, chronic kidney disease, diabetes mellitus, and immunocompromising conditions [3, 4].

Although the incidence of severe RSV illness is highest in infants, young children, and older adults [5], there is also a substantial and underestimated burden due to RSV in adults <60 years of age, especially among those with risk factors for severe disease [6–10]. A systematic review and meta-analysis of studies investigating medically attended RSV events among US adults reported underdetection-adjusted hospitalization incidences of 67/100 000 and 13/100 000 for those 50–64 and 18–49 years of age, respectively [7]. After adjustment for underdetection, emergency department admission rates and outpatient visits were respectively 110/100 000 and 1722/100 000 for those 50–64 years of age and 198/100 000 and 1401/100 000 for those 18–49 years of age. Consistent with these findings on rates of medically attended RSV events, in 2022, the annual economic burden in the United States due to RSV-associated hospitalization in adults 50–59 years of age was estimated to be US$1.1 billion [6].

After RSV infection, only a relatively short duration of natural immunity occurs [11, 12], and management consists

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primarily of supportive care. The bivalent RSV prefusion F protein-based (RSVpreF) vaccine received regulatory approvals in adults ≥60 years old on the basis of efficacy and safety data from the pivotal phase 3 study, which demonstrated vaccine efficacy of 89% against RSV-associated lower respiratory tract illness (LRTI) with ≥3 signs or symptoms at the end of the first RSV season [13, 14]. RSVpreF is also approved for maternal immunization to protect infants from birth to 6 months old on the basis of efficacy and safety data from a pivotal study in pregnant individuals [2, 14, 15].

There is an important need to evaluate the ability of RSVpreF to protect adults <60 years of age who are at high risk of severe RSV disease or complications from RSV disease, as well as immunocompromised adults. Adults with certain serious underlying chronic diseases, including cardiac, renal, and respiratory diseases, and diabetes mellitus, have elevated rates of RSV-associated illness, hospitalizations, and in-hospital fatalities compared with individuals without these conditions [16]. The impact of RSV disease on this population is likely underestimated because of lack of systematic diagnostic systems and robust surveillance. Additionally, management of RSV disease in adults is currently supportive.

The pivotal phase 3 RENOIR study of RSVpreF enrolled participants ≥60 years of age who were healthy or had stable chronic medical conditions (adults <60 years of age or those with immunocompromise were not included) [17]. Here we evaluate the safety, tolerability, and immunogenicity of RSVpreF in adults 18–59 years of age who are at high risk of severe RSV disease due to certain chronic medical conditions, including pulmonary, cardiovascular, and renal disease, and metabolic disorders, such as diabetes mellitus.

METHODS

Objectives, Participants, and Oversight

This study was part of a phase 3 trial assessing RSVpreF safety, tolerability, and immunogenicity in adults at high risk of severe RSV disease (NCT05842967). In this randomized, double-blind, placebo-controlled study, adults 18–59 years of age considered to be at high risk of severe RSV disease due to certain chronic medical conditions, including chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus, hyperthyroidism, and hypothyroidism) were enrolled. Definitions of chronic conditions and other eligibility criteria, as well as ethical conduct of the study, are summarized in the Supplementary Appendix.

Participants were randomized 2:1 to receive a single intramuscular injection of RSVpreF 120 µg (containing 60 µg each of RSV-A and RSV-B antigens) or placebo (lyophile match containing RSVpreF excipients).

Immunogenicity

Immunogenicity elicited 1 month after receipt of RSVpreF in adults with high-risk chronic medical conditions in this study (18–59-year-old group) was bridged to that in randomly selected ≥60-year-old participants from the immunogenicity subset who received RSVpreF in the pivotal RENOIR study (≥60-year-old group), in which RSVpreF efficacy was demonstrated [17]. The primary immunogenicity objective was to demonstrate that RSVpreF-elicited immune responses in the 18–59-year-old group were noninferior to those in the ≥60-year-old group. Participants had blood drawn before and 1 month after study vaccination for immunogenicity assessments. Neutralizing titers for RSV-A and RSV-B were measured for each blood sample at each time point as described previously [18, 19].

For immunobridging assessments, sera collected from the 18–59-year-old group were tested concurrently with sera from the ≥60-year-old group at all time points. The primary comparison for the immunobridging primary objective included RSV-A and RSV-B geometric mean titer (GMT) ratios (GMRs; 18–59-year-old group with the ≥60-year-old group) 1 month after vaccination and comparison of seroresponses, defined as ≥4-fold rise from baseline or ≥4 times the lower limit of quantitation (LLOQ) if baseline measurements were <LLOQ, 1 month after vaccination. Geometric mean fold rise (GMFR) from before to 1 month after vaccination was a secondary immunogenicity assessment in the 18–59-year-old group.

Safety

The primary safety objective was to describe the safety profile of RSVpreF, including local reactions, systemic events, adverse events (AEs), newly diagnosed chronic medical conditions (NDCMCs), serious AEs (SAEs), and AEs of special interest (AESIs; which included diagnoses of Guillain-Barré syndrome, acute polyneuropathy, atrial fibrillation, preterm delivery, and hypertensive pregnancy disorders). Local reactions and systemic events were recorded by participants in an electronic diary for up to 7 days after vaccination. AEs were reported through 1 month after vaccination and NDCMCs, SAEs, and AESIs throughout study participation (ie, 6 months after vaccination). An independent data monitoring committee reviewed unblinded safety data at regular intervals throughout the study.

Statistical Analysis

Study populations are defined in Supplementary Table 1. The sample size was based on demonstrating noninferiority with respect to RSV-A and RSV-B serum neutralizing titers from participants who received RSVpreF compared with serum blood samples taken from a random selection from a subset of RSVpreF-vaccinated older adults from the pivotal RENOIR study (≥60-year-old group) using a 1.5-fold noninferiority margin for GMR and a −10% noninferiority margin for difference in seroresponse rate for both RSV-A and

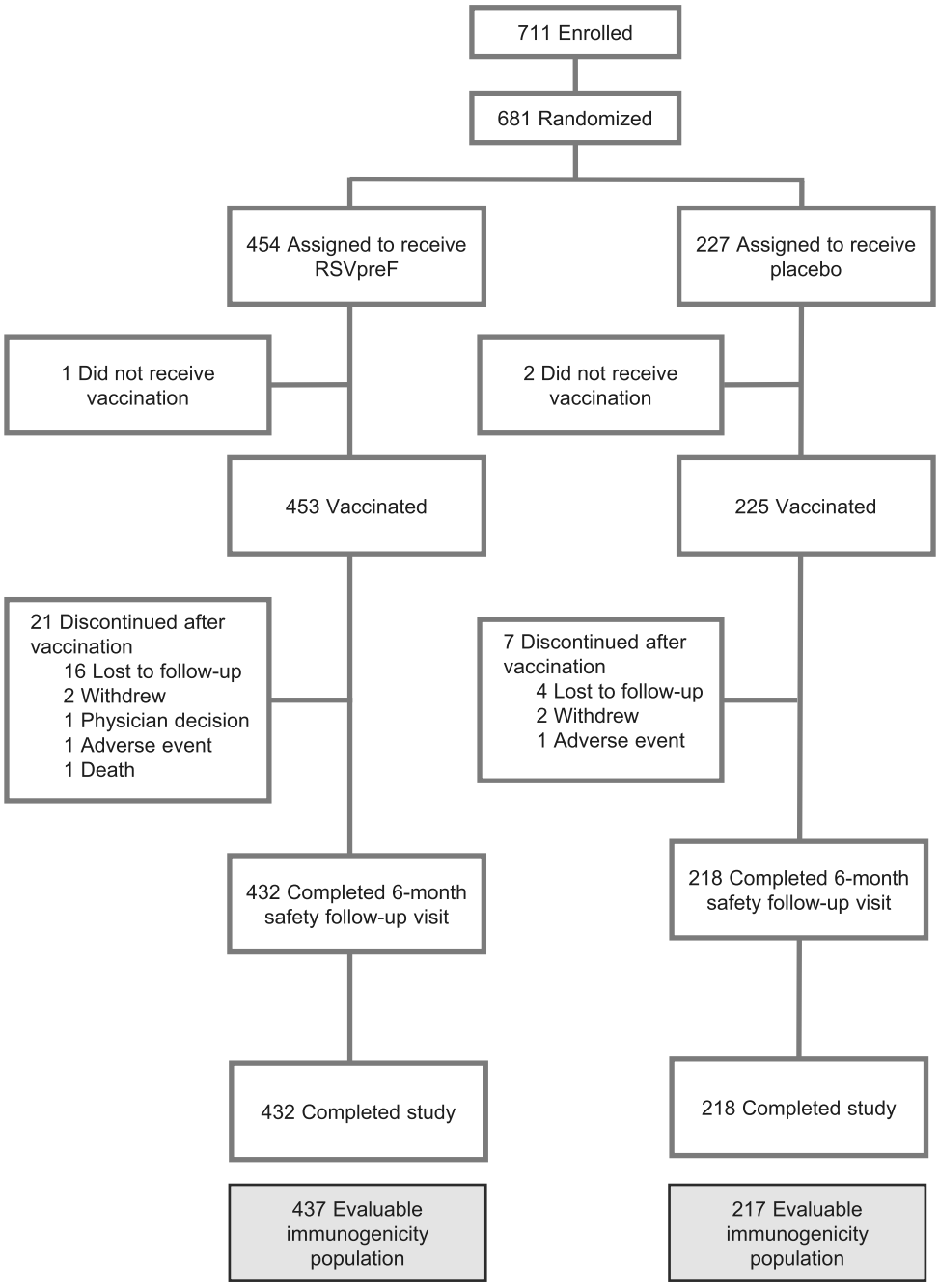


Figure 1. Enrollment, randomization, vaccine and placebo administration, and follow-up. The evaluable immunogenicity population is defined in Supplementary Table 1.

RSV-B. Noninferiority was declared if both the lower bounds of the 95% confidence interval (CI) adjusted GMRs were >.667 and the lower bounds of the 95% CIs of seroresponse rates differences were greater than −10% for both RSV-A and RSV-B (ie, a total of 4 comparisons). Primary analyses for the comparison of GMT for RSV-A and RSV-B serum neutralizing titers included model-adjusted GMRs at 1 month after vaccination, based on an analysis of covariance model with logarithmically transformed assay results at 1 month after vaccination as dependent variables, including age groups (18–59 years vs ≥60 years), baseline assay results (in a logarithmic scale), and sex because of known differences between the 2 age groups. Differences in seroresponse are expressed as a percentage with Miettinen-Nurminen 95% CIs. GMFRs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises with corresponding CIs based on the Student *t* distribution. GMTs and GMFRs are summarized by age subgroup (18–49 and 50–59 years), sex, race, ethnicity,

and prespecified medical conditions. Safety endpoints are presented using descriptive statistics and presented with Clopper-Pearson 95% CIs.

RESULTS

Participants

From 11 May 2023 to 21 September 2023, 681 participants were randomized at 27 US sites with 453 participants receiving RSVpreF and 225 receiving placebo (Figure 1). Most participants (95.4%) completed the 6-month safety follow-up visit (RSVpreF, n = 432; placebo, n = 218); the most common reason for discontinuation was lost to follow-up. The median age at vaccination was 49 years and 60.8% of participants were female, 68.4% White, 24.0% Black, and 22.1% Hispanic/Latino (Table 1). The most common medical conditions predisposing to increased risk of severe RSV illness were diabetes mellitus (RSVpreF, 41.7%; placebo, 44.9%), asthma (43.7%; 39.1%), and other metabolic disease (20.1%; 22.7%); 37.9% of participants were current or former tobacco users (39.5%; 34.6%). Demographic characteristics were similar in the evaluable immunogenicity population (Supplementary Table 2).

Immunogenicity

Demographic characteristics of 18–59-year-old participants from this study and ≥60-year-old participants from the pivotal RENOIR trial and included in the primary immunogenicity analysis are presented in Supplementary Table 3. Noninferiority criteria were met for all 4 coprimary immunogenicity endpoints (Figure 2). One month after vaccination with RSVpreF, the noninferiority criteria were met for the model-adjusted GMRs of high-risk adults 18–59 years of age versus adults ≥60 years of age (lower bounds of the 2-sided 95% CIs >.667) for both RSV-A and RSV-B. One month after vaccination with RSVpreF, noninferiority criteria were also met for differences in seroresponse rates for high-risk adults 18–59 years old versus adults ≥60 years old (lower bounds of the 2-sided 95% CIs > −10% for both RSV-A and RSV-B). The percentages of participants achieving a seroresponse were higher for high-risk adults 18–59 years old (RSV-A, 93.1%; RSV-B, 93.4%) than adults ≥60 years old (RSV-A, 88.0%; RSV-B, 85.0%).

Neutralizing GMTs for RSV-A and RSV-B increased substantially from before vaccination to 1 month after vaccination for high-risk adults 18–59 years old who received RSVpreF, with GMFRs ≥17.5 (Figure 3). Observations across subgroups of age, sex, race, ethnicity, and prespecified medical conditions were generally similar. Notably, immune responses after RSVpreF were similar for those 18–49 and 50–59 years old (GMFRs from before to 1 month after vaccination, 17.0–17.9 for RSV-A and 18.4–18.7 for RSV-B).

Table 1. Demographic and Clinical Characteristics of Participants in the Safety Population

Characteristic	RSVpreF (N[a] = 453)	Placebo (N[a] = 225)	Total (N[a] = 678)
Age, y			
Mean (SD)	46.8 (9.9)	46.4 (10.5)	46.7 (10.1)
Median (range)	49.0 (18, 59)	49.0 (20, 59)	49.0 (18, 59)
Sex, n (%)			
Male	193 (42.6)	73 (32.4)	266 (39.2)
Female	260 (57.4)	152 (67.6)	412 (60.8)
Race, n (%)			
White	312 (68.9)	152 (67.6)	464 (68.4)
Black	106 (23.4)	57 (25.3)	163 (24.0)
Asian	24 (5.3)	9 (4.0)	33 (4.9)
Multiracial	3 (0.7)	1 (0.4)	4 (0.6)
Native Hawaiian or other Pacific Islander	2 (0.4)	1 (0.4)	3 (0.4)
American Indian or Alaska Native	1 (0.2)	0	1 (0.1)
Not reported	5 (1.1)	5 (2.2)	10 (1.5)
Ethnicity, n (%)			
Hispanic or Latino	102 (22.5)	48 (21.3)	150 (22.1)
Not Hispanic or Latino	348 (76.8)	175 (77.8)	523 (77.1)
Not reported	3 (0.7)	2 (0.9)	5 (0.7)
With ≥1 prespecified medical condition,[b] n (%)	453 (100.0)	223 (99.1)	676 (99.7)
>1 prespecified medical condition	147 (32.4)	68 (30.2)	215 (31.7)
Chronic pulmonary conditions	239 (52.8)	116 (51.6)	355 (52.4)
COPD	25 (5.5)	11 (4.9)	36 (5.3)
Asthma	198 (43.7)	88 (39.1)	286 (42.2)
Other lung disease	47 (10.4)	26 (11.6)	73 (10.8)
Cardiovascular conditions	38 (8.4)	16 (7.1)	54 (8.0)
Chronic heart failure	9 (2.0)	3 (1.3)	12 (1.8)
Coronary artery disease	19 (4.2)	4 (1.8)	23 (3.4)
Other heart disease	19 (4.2)	12 (5.3)	31 (4.6)
Diabetes mellitus	189 (41.7)	101 (44.9)	290 (42.8)
Other	139 (30.7)	68 (30.2)	207 (30.5)
Liver disease	20 (4.4)	13 (5.8)	33 (4.9)
Renal disease[c]	17 (3.8)	4 (1.8)	21 (3.1)
Neurologic disease	16 (3.5)	1 (0.4)	17 (2.5)
Hematologic disease	6 (1.3)	7 (3.1)	13 (1.9)
Other metabolic disease[d]	91 (20.1)	51 (22.7)	142 (20.9)
Tobacco use, n (%)			
Current	78 (17.2)	39 (17.3)	117 (17.3)
Former	101 (22.3)	39 (17.3)	140 (20.6)
Never	274 (60.5)	147 (65.3)	421 (62.1)
Baseline respiratory rate (breaths/min), n (%)			
Mean (SD)	15.6 (1.9)	15.7 (2.0)	15.6 (2.0)
Median	16.0	16.0	16.0

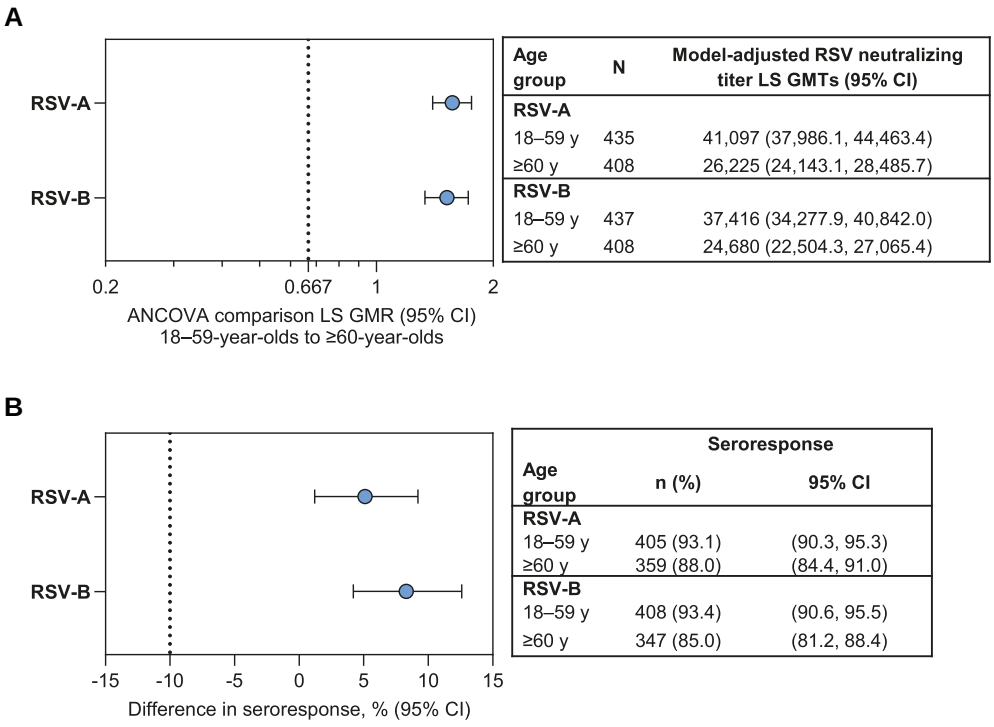
Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation.

[a]N is the number of participants in the specified vaccine group; this value is the denominator for the percentage calculations.

[b]Two participants were vaccinated but did not have ≥1 prespecified medical condition.

[c]Individuals with end-stage renal disease with or without dialysis were excluded from this study.

[d]The conditions in this category were hypothyroidism (n = 118), hyperthyroidism (n = 9), Hashimoto's thyroiditis (n = 9), metabolic syndrome (n = 5), Graves' disease (n = 3), and hypercortisolism (n = 1); 3 participants had 2 of these conditions (ie, 1 participant with metabolic syndrome and hypothyroidism and 2 participants with Hashimoto's thyroiditis and hypothyroidism).



Age group	N	Model-adjusted RSV neutralizing titer LS GMTs (95% CI)
RSV-A		
18–59 y	435	41,097 (37,986.1, 44,463.4)
≥60 y	408	26,225 (24,143.1, 28,485.7)
RSV-B		
18–59 y	437	37,416 (34,277.9, 40,842.0)
≥60 y	408	24,680 (22,504.3, 27,065.4)

	Seroresponse	
Age group	n (%)	95% CI
RSV-A		
18–59 y	405 (93.1)	(90.3, 95.3)
≥60 y	359 (88.0)	(84.4, 91.0)
RSV-B		
18–59 y	408 (93.4)	(90.6, 95.5)
≥60 y	347 (85.0)	(81.2, 88.4)

Figure 2. RSV-A and RSV-B neutralization titer (*A*) and seroresponse results (*B*) at 1 m after RSVpreF vaccination in participants 18–59 y of age versus adults ≥60 y of age. Results are for the evaluable immunogenicity population (Supplementary Table 1). Participants ≥60 y of age are a subset of participants who received RSVpreF in the pivotal RENOIR study. The LLOQ values were 242 for RSV-A and 99 for RSV-B neutralizing titers. Assay results below the LLOQ were set to 0.5 × LLOQ. GMTs and GMRs and associated 2-sided CIs were calculated by exponentiating the LS means or the mean difference, respectively, and the corresponding CIs based on analysis of log-transformed titers using a regression model with 18–59 y of age and ≥60 y of age groups, baseline log-transformed titers, and sex as covariates. Seroresponse was defined as achieving a ≥4-fold rise from baseline (before vaccination) or a postvaccination assay result ≥4 × LLOQ if the baseline measurement was <LLOQ. Seroresponses are presented with Clopper-Pearson exact 2-sided 95% CIs. Difference in seroresponse is expressed as a percentage with Miettinen-Nurminen 95% CIs. The dotted lines represent the prespecified noninferiority criteria. Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; GMR, geometric mean ratio; GMT, geometric mean titer; LLOQ, lower limit of quantitation; LS, least square; RSV, respiratory syncytial virus.

Safety

RSVpreF recipients reported more local reactions than placebo recipients (RSVpreF, 36.6%; placebo, 11.6%), whereas systemic event rates were generally similar between study groups (RSVpreF, 57.4%; placebo, 55.6%; Figure 4). Local reactions and systemic events were generally mild to moderate; severe events occurred in ≤2.0% of participants in each group. For the RSVpreF group, median onset of reactogenicity events was 2–3 days and median duration was 1–2 days; corresponding onset and duration in the placebo group was 1–5 and 1–2 days. Injection-site pain was the most common local reaction (RSVpreF, 35.3%; placebo, 10.7%), and fatigue (RSVpreF, 37.3%; placebo, 38.2%) was the most common systemic event. Muscle pain was reported in 24.4% of RSVpreF recipients and 16.0% of placebo recipients. Fever occurred in 1.6% of RSVpreF recipients and 1.3% of placebo recipients, and no fever >38.9°C was reported.

The frequency of AEs to 1 month after vaccination were similar in the RSVpreF (7.1%) and placebo groups (7.6%), and most were mild or moderate in severity (Figure 5). AEs in the infections and infestations category were the most common (RSVpreF, 3.1%; placebo, 4.0%). An AE assessed by the investigator as related to study intervention was reported by 1 participant in the RSVpreF group (mild nonserious urticaria resolving in 2 days). Severe AEs to 1 month after vaccination were reported by 0.2% and 1.8% of RSVpreF and placebo recipients, respectively; none were assessed as being vaccine-related by the investigator. SAEs through 6 months after vaccination were reported in 1.1% and 3.1% of RSVpreF and placebo recipients, respectively (Supplementary Table 4); none were assessed as related to study vaccination. Overall, 0.7% and 2.2% of RSVpreF and placebo recipients reported NDCMCs; none were assessed by the investigator as related to study intervention. No AESIs (including in 1 participant in the RSVpreF group who had exposure during pregnancy), study intervention-related AEs leading to withdrawal, or study intervention-related deaths were reported. One death was reported in an RSVpreF recipient (cardiorespiratory arrest on Day 106 in a 50–59-year-old participant that was assessed as not related to vaccination by the investigator).

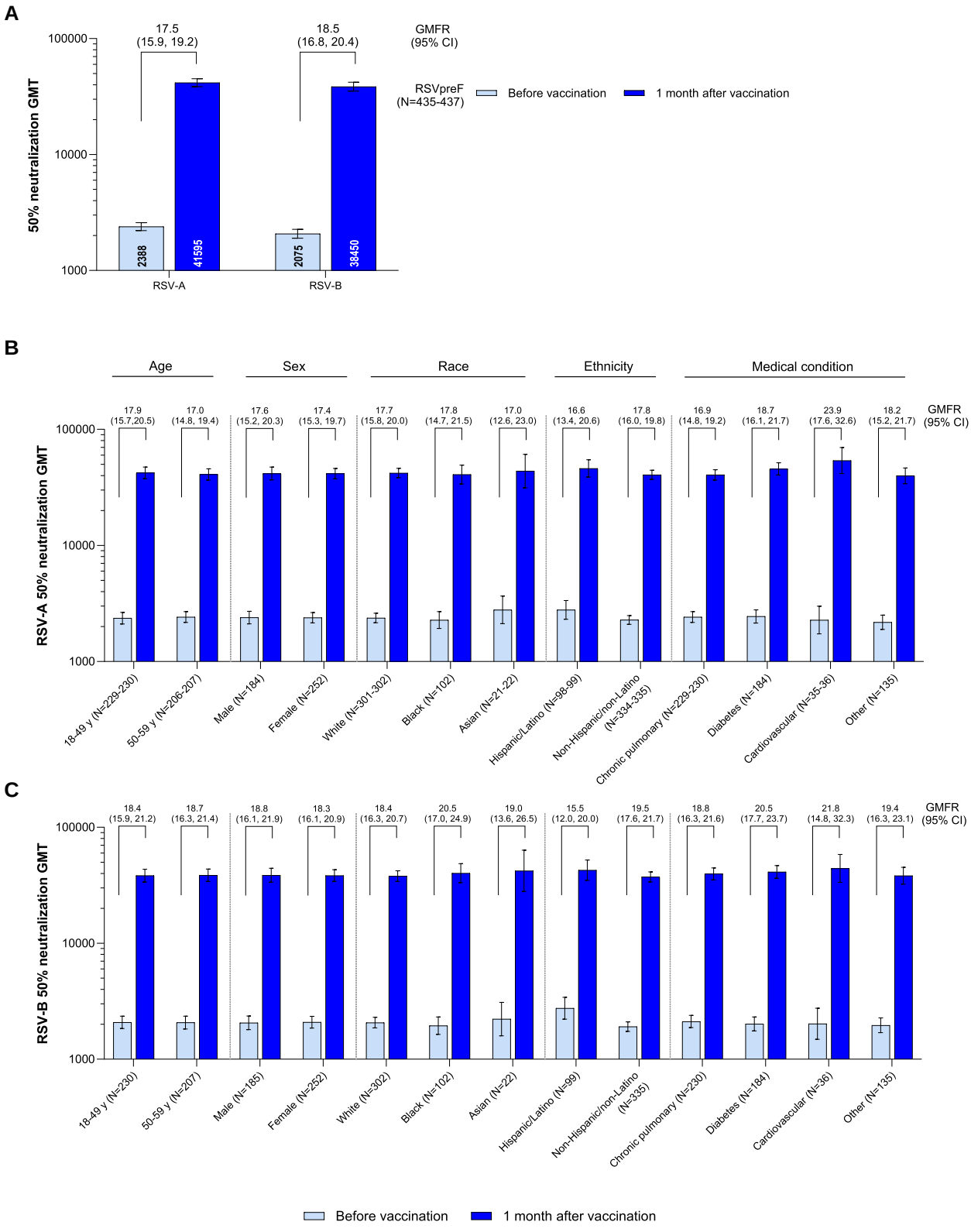


Figure 3. RSV neutralizing titer GMTs and GMFRs with 95% CIs (*A*) overall and by demographic subgroup for (*B*) RSV-A, and (*C*) RSV-B. Data are for the evaluable immunogenicity population (Supplementary Table 1). LLOQ values were 242 for RSV-A and 99 for RSV-B neutralizing titers. Assay results below the LLOQ were set to 0.5 × LLOQ for all GMT and GMFR calculations, except when the prevaccination assay result was <LLOQ and the postvaccination result was ≥LLOQ, in which case the prevaccination value was set to LLOQ when calculating GMFRs. GMTs and GMFRs were calculated by exponentiating the mean logarithm of the titers or the mean logarithm of the fold rises, respectively, with corresponding CIs based on the Student *t* distribution. Panels *B* and *C* include subgroups with ≥3 participants. Abbreviations: CI, confidence interval; GMFR, geometric mean fold rise; GMT, geometric mean titer; LLOQ, lower limit of quantitation; N, number of participants with valid and determinate assay results; RSV, respiratory syncytial virus.

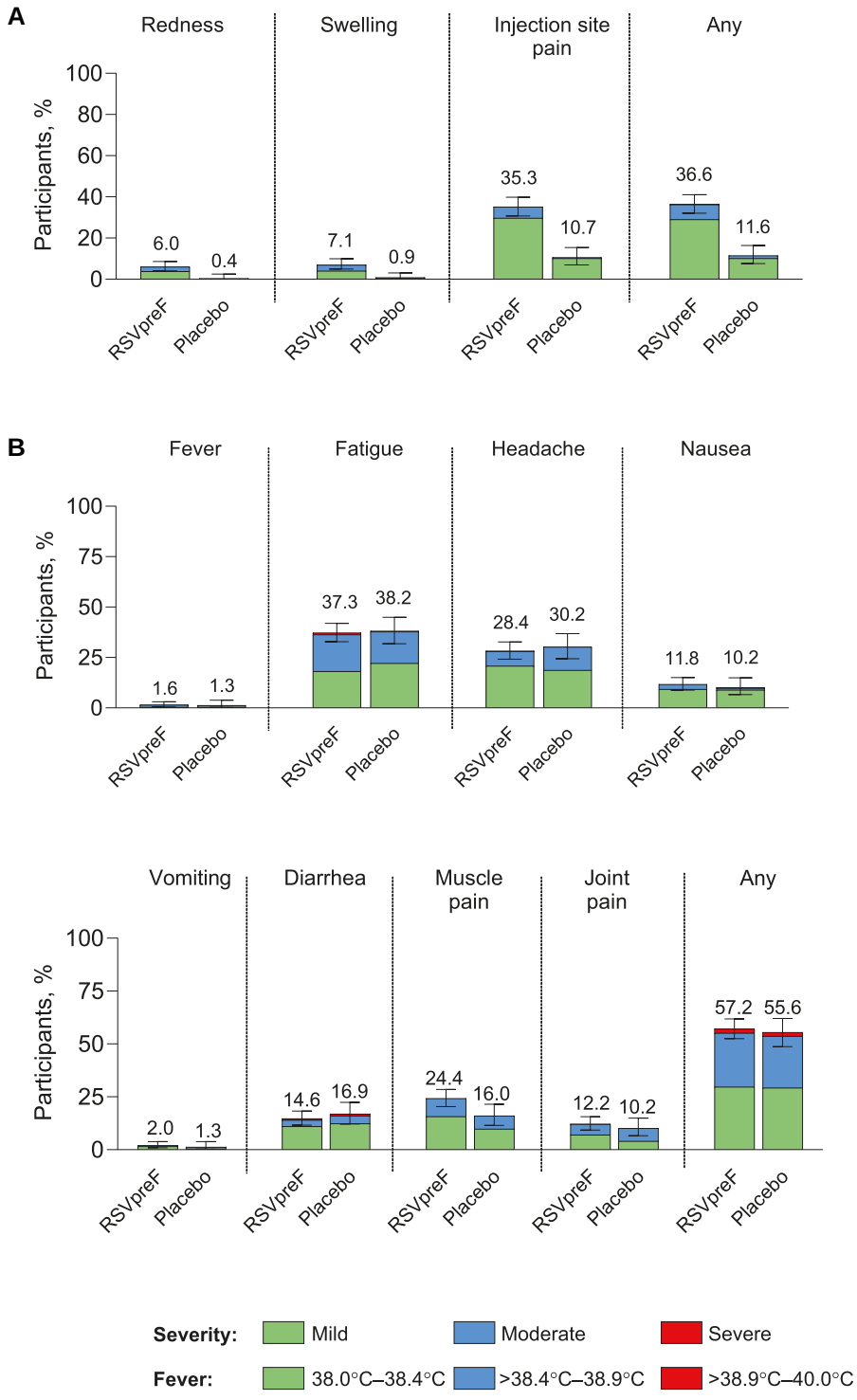


Figure 4. Local reactions and systemic events reported within 7 d after administration of RSVpreF or placebo. Panel *A* shows local reactions, and panel *B* shows systemic events in RSVpreF (n = 451) and placebo recipients (n = 225) who received study intervention and who had ≥1 d of electronic data transferred. Severity scales are summarized in Supplementary Table 5. The numbers above the bars show the percentage of participants in each group with the specified local reaction or systemic event. Error bars are 95% CIs. Severe swelling was reported by 1 participant (0.2%) in the RSVpreF group; severe fatigue in 4 participants (0.9%) in the RSVpreF group and 1 participant (0.4%) in the placebo group; severe headache in 1 participant (0.2%) in the RSVpreF group; severe joint pain in 1 participant (0.2%) in the RSVpreF group; severe nausea in 1 participant (0.4%) in the placebo group; and severe diarrhea in 3 participants (0.7%) in the RSVpreF group and 2 participants (0.9%) in the placebo group. Abbreviation: CI, confidence interval.

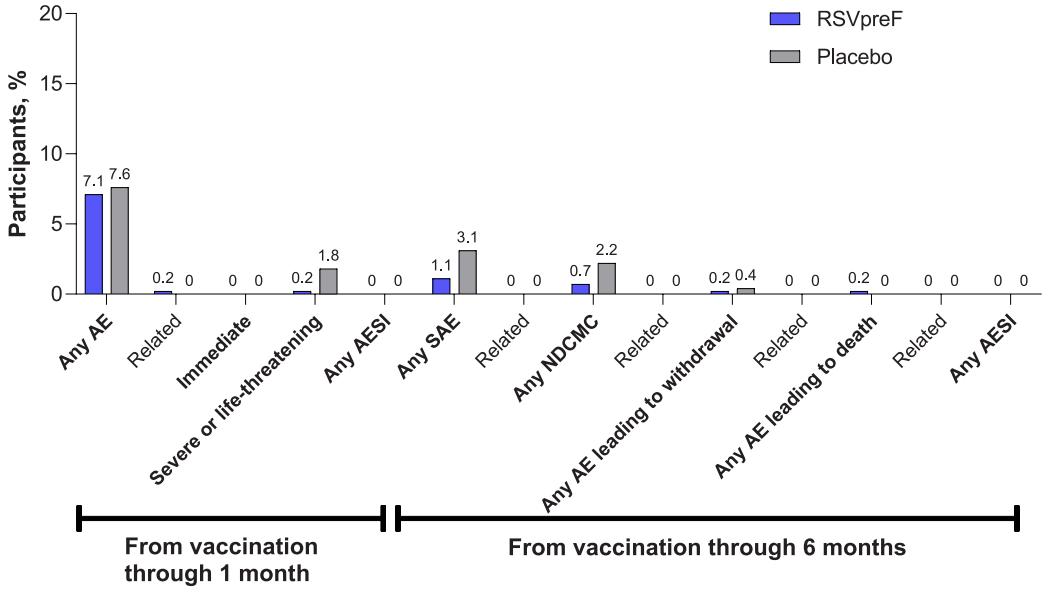


Figure 5. Adverse events. Data are for the safety population (defined in Supplementary Table 1). Related events were as determined by the investigator. Abbreviations: AE, adverse event; AESI, adverse event of special interest; NDCMC, newly diagnosed chronic medical condition.

DISCUSSION

RSV is an important respiratory pathogen both in older adults and in adults <60 years of age, particularly those with risk factors for severe disease [6–8, 10]. A global meta-analysis including data predominantly from Europe, North America, and Australasia reported that among adults ≥18 years of age with comorbidities, RSV caused 7.03% (95% CI: 5.18–9.48) of symptomatic respiratory infections in annual studies and 7.69% (95% CI: 6.23–9.46) in seasonal studies [20]. Adults with cardiovascular and respiratory comorbidities have a substantially higher risk of RSV-associated hospitalization compared with those without [8, 10]. In a German study from 2015–2018, patients 18–59 years of age with risk factors (including congestive heart failure [CHF], arrhythmia, ischemic heart disease, and chronic obstructive pulmonary disease [COPD]) were 3.3–6.2 times more likely to be hospitalized due to RSV than those without [10]. A US study from 2017–2020 reported that in patients <60 years of age with CHF, RSV-associated hospitalization rates were 13–33 times those without, whereas other conditions (including asthma, COPD, and diabetes mellitus) also substantially increased the risk of hospitalization [8]. Collectively, these data highlight the important unmet need to prevent RSV illness in adults <60 years of age with risk factors who are currently not eligible for vaccinations against RSV.

In the current study of 18–59-year-olds with risk factors for severe RSV illness, a single dose of RSVpreF elicited robust RSV-A and RSV-B neutralizing responses met the primary immunobridging endpoints to that in adults ≥60 years of age from the pivotal RENOIR study in which efficacy against RSV illness was demonstrated [17]. The safety and tolerability of RSVpreF in this population was acceptable and consistent with previous studies of RSVpreF [15, 17].

All 4 primary noninferiority immunogenicity objectives were met for RSV-A and RSV-B for the model-adjusted GMRs and for the difference in seroresponse rates of high-risk adults 18–59 years of age versus adults ≥60 years of age from the pivotal RENOIR study. Immunobridging is an approach that uses immunogenicity data to infer vaccine effectiveness [21]. The pivotal RENOIR study in adults ≥60 years of age demonstrated vaccine efficacy of 89% against severe RSV-associated LRTI [13, 14]. On the basis of the noninferiority of immune responses to the adults in the pivotal RENOIR trial, it is therefore reasonable to infer that RSVpreF will also be effective against severe RSV in high-risk adults 18–59 years of age.

In the descriptive secondary immunogenicity analyses, strong immune responses were elicited by RSVpreF in high-risk adults 18–59 years of age and across subgroups suggesting no clinically meaningful differences by age (ie, 18–49 vs 50–59 years of age), sex, race, ethnicity, and prespecified medical conditions in GMTs or GMFRs after a single dose of RSVpreF. Notably, immune responses after RSVpreF were similar for high-risk adults 18–49 years and 50–59 years of age.

The safety and side-effect profiles of RSVpreF in 18–59-year-olds with risk factors for severe RSV illness were consistent with those in previous adult studies [15, 17]. Most

local reactions and systemic event rates were mild or moderate in severity and, apart from injection-site pain, which was more common in RSVpreF recipients, were generally similar between groups. AEs were infrequent and reported at similar rates in the RSVpreF and placebo groups, and the incidence of severe AEs was low. Only one AE was considered to be related to RSVpreF (nonserious urticaria).

A limitation of this study is the exclusion of participants with immunocompromising conditions; however, this group, which includes individuals with end-stage renal disease who are undergoing hemodialysis therapy, is included in another part of the same trial for which results will be reported separately. This study also did not assess the severity of the underlying medical condition potentially affecting the generalizability of the results. Additionally, some of the immunogenicity subgroups included a limited number of participants; therefore, the results should be interpreted with caution. Nevertheless, the results were generally consistent across subgroup analyses in spite of small samples sizes in some groups and suggested no clinically meaningful differences. Although the noninferiority immunogenicity analyses were performed with concurrent testing of sera from 18−<59-year-old participants and ≥60-year-old participants from RENOIR, the analysis did not use a contemporaneously enrolled cohort of older adults (RENOIR enrolled participants from August 2021 [17], whereas this study enrolled participants from May 2023). Finally, persistence of immune responses was not investigated, although in RENOIR, efficacy has been demonstrated through 2 RSV seasons.

In conclusion, study results support the expansion of the RSVpreF indication for prevention of RSV-associated LRTI to include adults 18 through 59 years of age with risk factors for severe RSV, thereby fulfilling the important unmet need in this population.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. M. D., S. M., W. H., and K. C. were involved in acquisition or generation of data. W. T. and M. M. L. were involved in acquisition or generation of data and data interpretation. E. D., F. R., M. P., H. W., and Z. M.-M. were involved in concept and study design, acquisition or generation of data, data interpretation, data analysis, and data verification. Q. J. and W. L. were involved in concept and study design, acquisition or generation of data, data interpretation, data analysis, data verification, and statistical analysis. U. S. and I. M. were involved in acquisition or generation of data, data interpretation, data analysis, and data verification. E. K. was involved in concept and study design, acquisition or generation of data, data analysis, and data verification. D. C., K. S., A. A., and A. G. were involved in concept and study design and data analysis. All authors critically reviewed the manuscript and approved the final draft.

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Data availability. Upon request and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

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Potential conflicts of interest. W. T. has received research grants paid to his institution from Pfizer, Moderna, Janssen, AstraZeneca, ViiV, Merck, Gilead, and GSK. E. D., Q. J., W. L., F. R., M. P., H. W., M. M. L., U. S., Z. M.-M., E. K., D. C., K. A. S., A. S. A., A. G., and I. M. are Pfizer employees and may hold stock or stock options. All other authors report no potential conflicts.

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