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Phase 2 Randomized Bivalent rsvpref Maternal Vaccine Trial: Final Safety, Antibody Persistence and Efficacy

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Background: This report summarizes the final results from a randomized, placebo-controlled, phase 2b trial evaluating safety, antibody persistence, and potential efficacy of a bivalent

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respiratory syncytial virus (RSV) prefusion F (RSVpreF) vaccine in pregnant individuals and their infants.

Methods: Maternal participants were randomized from 24−36 weeks gestation to receive RSVpreF (120 or 240 μg ± aluminum hydroxide) or placebo.

Results: This analysis included 579 pregnant individuals and 572 infants from 4 countries (Argentina, Chile, South Africa, United States); 462 maternal participants received RSVpreF. Adverse events in the month following vaccination (maternal) or birth (infant) were mostly anticipated events in pregnancy and the neonatal period, respectively. For all RSVpreF groups, combined RSV-A/-B 50% neutralizing titers peaked 2 weeks after vaccination. At delivery, geometric mean titer ratios between RSVpreF and placebo recipients' infants were 10.9−13.6. Transplacental transfer ratios (all groups) were 1.39−1.83. Neutralizing geometric mean titers remained higher in infants whose mothers received RSVpreF versus placebo through their first 6 months of life, with an estimated half-life of 39−44 days. In an exploratory analysis, observed efficacy (95% confidence interval) for the combined RSVpreF groups against medically attended and severe medically attended infant RSV lower respiratory tract illness through the first 180 days of life was 75% (−11%, 94%) and 83% (−48%, 99%), respectively.

Conclusions: RSVpreF had a favorable safety profile and elicited robust neutralizing responses with efficient transplacental transfer. The potential to prevent infant RSV-associated lower respiratory tract illness was subsequently confirmed in the pivotal phase 3 efficacy trial. (NCT04032093)

Key words: Vaccines; RSV; Pregnancy

INTRODUCTION

Respiratory syncytial virus (RSV)-associated illness is a leading cause of infant mortality, particularly among children <6 months of age and in low- and middle-income countries (LMICs), and accounts for a substantial proportion of infant hospitalizations in high-income regions [1,2]. Therefore, protecting infants in the first months of life against RSV-associated illness, including through maternal vaccination, is critical.

RSVpreF (ABRYSVO™) is a bivalent RSV prefusion F subunit vaccine comprised of equal quantities of stabilized prefusion F antigens from RSV-A and RSV-B (60-μg each [120-μg total dose]), which are the 2 cocirculating RSV subgroups [3]. RSVpreF is licensed and recommended for maternal vaccination in the United States, European Union, and many other countries [4-6]. As part of the clinical development program for maternal RSVpreF vaccination and in preparation for the pivotal phase 3 MATISSE efficacy study that supported this licensure, we conducted a global phase 2b study of RSVpreF in healthy pregnant individuals and their infants. An interim analysis showed the vaccine had an acceptable safety profile, produced robust neutralizing antibody

responses with efficient transplacental transfer to infants, and provided preliminary evidence of efficacy against RSV-associated illness in infants [7]. Here we report the final safety, immunogenicity, and exploratory efficacy results of this study, as well as antibody levels in infants through 6 months of age.

METHODS

Study design and participants

We assessed RSVpreF safety and immunogenicity in healthy pregnant individuals and their infants in Argentina, Chile, South Africa, and the United States. Participants were eligible for inclusion in this phase 2b, randomized, placebo-controlled, observer-blinded study if they were 18−49 years of age and 24−36 weeks' gestation on the day of planned vaccination, with an uncomplicated, singleton pregnancy, and whose fetus had no significant abnormalities observed on ultrasound. Because of reported disparities in health outcomes by race and ethnicity, no restriction was placed on participant enrollment by these demographic characteristics. Infants were eligible for inclusion if the parent provided informed consent, and parents could comply with scheduled visits, the study plan, and study procedures.

Eligible maternal participants were randomized (1:1:1:1:1 ratio) to receive either a single intramuscular injection of 120 µg or 240 µg of RSVpreF formulated with or without aluminum hydroxide [$Al(OH)_3$], or a single intramuscular injection of placebo. Further details on randomization and blinding are provided in the **Supplementary Material**.

Vaccination of pregnant individuals was planned before the onset of the RSV season in each hemisphere, so infants were likely to be exposed to RSV during their first 6 months of life. Individuals participated from enrollment during pregnancy, and for approximately 12 months after delivery of their infants (up to approximately 17 months depending on gestational age [GA] at vaccination). Infants participated from birth through approximately 12 months of age.

Northern Hemisphere (United States) maternal vaccination occurred between August 12, 2019, and November 6, 2019, with the last infant born on February 24, 2020. Southern Hemisphere (Argentina, Chile, South Africa) maternal vaccination occurred between January 29, 2020, and July 2, 2020, with the last infant born on October 10, 2020 (in South Africa). However, COVID-19 pandemic restrictions affected enrollment and study execution at Southern Hemisphere sites, with <50% of planned maternal enrollment achieved. Study and serology completion dates were September 30, 2021, and January 5, 2022, respectively.

The ethical conduct of the study is provided in the **Supplementary Material**. Complete eligibility criteria and protocol amendments during study conduct are available with the protocol on ClinicalTrials.gov (NCT04032093).

Objectives and outcomes

Primary, secondary, and exploratory study outcomes are summarized in **Table S1**. Safety outcomes included in this final analysis were unsolicited adverse events (AEs) for the month after vaccination (maternal participants) or first month of life (infant participants), and serious AEs (SAEs), medically attended AEs (MAEs), and AEs of special interest (AESIs; ie, congenital anomalies, developmental delay, preterm birth) for the duration of participation in the study. Reactogenicity events collected within 7 days after study vaccination were reported previously [7]. Stopping rules are described in the **Supplementary Material**.

Immunogenicity objectives included description of RSVpreF-elicited immune responses. Maternal participants had blood drawn for serology assessments before vaccination, 2 weeks and 1 month after vaccination, at delivery, and 6 months after delivery. For infants, umbilical cord blood was collected at birth, and blood samples were obtained at 1, 2, 4, and 6 months of age; to reduce numbers of blood draws for individual infants, infants were randomized to have blood drawn at 1 and 4 months or 2 and 6 months of age. Serum neutralizing titers were determined in qualified RSV-A and RSV-B neutralization assays using the RSV-A M37 strain (Meridian Life Science, Memphis, TN, USA) and RSV-B B18537 strain (ATCC, Manassas, VA, USA) as described previously [8,9], and reported as 50% geometric mean neutralizing titers. Determination of neutralizing antibody half-life is outlined in the **Supplementary Material**. As a post hoc assessment of potential protective neutralizing titers in infants, serum concentrations for palivizumab (~100 μg/mL) and nirsevimab (6.8 μg/mL) shown to confer protection in preventing RSV-associated illness were constructed as reference points, which has been described previously for nirsevimab [10]. The palivizumab concentration is associated with 100% protection against RSV-associated pediatric intensive care unit (ICU) admission [11]. The nirsevimab concentration is reported as the 90% effective concentration threshold where 70% efficacy against medically attended RSV-associated lower respiratory tract illness (LRTI) through 150 days after monoclonal antibody (mAb) administration in infants was observed [12-14]. Serum concentrations in 97.9% of infants (with available data) of nirsevimab recipients were >6.8 μg/mL 90% effective concentration 151 days after mAb administration [12]. Palivizumab and nirsevimab assays used qualified and validated RSV neutralizing assays which included the same viral strains, cell lines, and primary antibody. Immunoglobulin G (IgG) levels against both RSV-A and RSV-B prefusion antigens in sera from maternal participants and their infants were also determined as an exploratory assessment using a direct-binding Luminex immunoassay as described previously [3], and reported as anti-prefusion F IgG concentrations.

Acute respiratory tract illness (RTI) surveillance in infant participants only was conducted through 6 months of age by weekly contact with parents/guardians. Infant RTI assessments included physical examination and collection of nasal swabs for reverse transcriptase-polymerase chain reaction. RSV-associated LRTI cases were determined by the presence of RSV from a nasal swab collected during acute RTIs meeting protocol-defined clinical criteria, following internal, blinded, independent adjudication panel review.

Statistical analysis

The study was not designed for formal hypothesis testing. Sample size was not determined by specific hypothesis testing and was chosen for likelihood of detecting AEs (further described in the **Supplementary Material**). No formal interim analysis was initially planned; however, the previously reported interim analysis was conducted per prespecified FDA guidance to support initiation of the phase 3 MATISSE trial [7].

Safety analyses are based on the safety population (defined in **Table S1**). Numbers and percentages of participants reporting each event and exact 2-sided Clopper-Pearson 95% CIs were provided by study group.

Immunogenicity analyses were based on evaluable populations (defined in **Table S1**). For maternal and infant participants, RSV-A and RSV-B neutralizing geometric mean titers (GMTs) were summarized descriptively for each study group, along with associated 2-sided 95% CIs. For maternal and infant participants, geometric mean ratios (GMRs) of neutralizing GMTs of the RSV vaccine group relative to the placebo group for the RSV-A and RSV-B neutralizing antibody titers at each available timepoint after vaccination were calculated, along with associated 2-sided 95% CIs. For combined RSV-A/-B neutralizing GMTs, the geometric means of RSV-A and RSV-B neutralizing titers were determined, and group geometric means and 95% CIs were calculated. Geometric mean fold rises (GMFRs) were calculated as the mean difference of an individual maternal participant's logarithmically transformed antibody levels (postvaccination minus prevaccination) and back transformed to the original units. For each individual, combined RSV-A/-B neutralizing fold rises were the geometric mean of the RSV-A and RSV-B fold rise. Associated 95% CIs for GMFRs were computed. Maternal-to-infant placental transfer ratios of RSV-A, RSV-B, and combined RSV-A/-B neutralizing antibody titers (paired mother−infant titers) and associated 95% CIs were also summarized. The IgG geometric mean concentration (GMCs) in maternal and infant participants at each available timepoint and geometric mean of maternal-to-infant placental transfer ratio of anti-prefusion F IgG concentration or paired mother−infant concentrations at delivery/birth were calculated and the associated 95% CIs were determined. Further details on the determination of immunogenicity measurements are provided in the **Supplementary Material**.

In an exploratory analysis, observed vaccine efficacy (VE) in infants was estimated as the percentage of infant participants with RSV-LRTI, along with the associated exact Clopper-Pearson 2-sided 95% CI. VE was summarized for the combined RSV vaccine groups for cumulative cases occurring through the first 6 months of life.

Immunogenicity and efficacy analyses were also descriptively assessed by geographic subgroup (ie, Northern and Southern Hemisphere). The statistical analysis plan is available at ClinicalTrials.gov (NCT04032093).

RESULTS

Participants

This final analysis includes 579 vaccinated pregnant individuals (462 of whom received RSVpreF) and 572 infants; of these infants, 540 had 6 months of follow-up and 519 completed the study (12 months follow-up; **Figures 1−2; Tables S2−S3**). Demographic characteristics of maternal participants were broadly similar across study groups (**Table S4**). Overall, approximately three quarters of maternal participants were White and 11.2% were from the Southern Hemisphere. At vaccination, the median age of maternal participants was 27 (range, 18–42) years and median GA was 30-3/7 (range, 24-0/7−36-1/7) weeks. Half of infant participants were female and 73.4% were White (**Table S5**). The median interval between vaccination and delivery was 60 (range, 7−124) days. Most infants were born at term; median GA at birth was 39.1 (range, 31.3−41.7) weeks.

Safety

AEs reported within 1 month after vaccination are summarized in **Figure 3A**. In this final analysis of participants from the Northern and Southern Hemispheres, the most frequently reported AEs by system organ class across all groups were infections and infestations (range, 6.0%−11.2%); pregnancy, puerperium, and perinatal conditions (3.5%−7.7%); and gastrointestinal disorders (1.7%−9.5%).

Most maternal participants had uncomplicated pregnancies and delivered vaginally (70.1%−79.1% across study groups) at full term (91.4%−96.6%); premature live deliveries (ie, <37 weeks GA) occurred in 25 (4.3%) maternal participants (RSVpreF groups, 3.4%−6.9%; placebo, 2.6%). Complications occurred during 47 (8.1%) deliveries and were reported with a similar frequency across all study groups (5.2%−11.1%). Obstetric complications were also reported with similar frequency across study groups including hypertensive disorders of pregnancy (pre-eclampsia and gestational hypertension, reported in 2.4% [11/462] and 1.3% [6/462] of RSVpreF recipients and 2.6% [3/117] and 3.4% [4/117] of placebo recipients, respectively; **Table S6**).

The AEs reported in infants within the first month of life are summarized in **Figure 3B**. One infant participant who received placebo was withdrawn because of complications resulting from complex congenital heart disease. Infant birth outcomes and AESIs are summarized in **Table 1**. Of 572 infants in the study, 25 (4.4%) were born prematurely (<37 weeks estimated GA; RSVpreF groups, 4.8%; placebo, 2.6%) of which 15 (2.6% of all births) were born in the 36th week (range, 31-3/7−36-6/7 weeks).

Immunogenicity and efficacy

RSVpreF induced robust RSV-A and RSV-B neutralizing titers in maternal participants following vaccination (**Figure 4A; Figure S1A**). The 50% neutralizing titers peaked by 2 weeks after RSVpreF receipt and gradually declined thereafter. Combined RSV-A/-B neutralizing GMTs in

maternal participants who received RSVpreF were higher than in those who received placebo from after dosing through 6 months after delivery, with GMRs between vaccine and placebo recipients ranging from 21.1−29.4 at 2 weeks after study vaccination, 12.0−15.9 at delivery, and 3.9−5.8 at 6 months after delivery (**Table S7**). Combined RSV-A/-B neutralizing titer GMFRs from before vaccination to the after vaccination timepoints in RSVpreF groups peaked at 20.8−27.7 at 2 weeks after vaccination and declined to 5.6−7.7 at 6 months after delivery (**Table S8**). Combined RSV-A/-B prefusion F binding IgG GMCs in maternal participants showed a similar pattern (**Figure S2A**).

Maternal antibodies were also efficiently transferred to infants and persistence of transferred antibody was observed through 6 months of life (**Figure 4B; Figure S1B**).

Combined RSV-A/-B neutralizing GMTs in infants whose mothers received RSVpreF were higher than in infants whose mothers received placebo, with GMRs between infants of RSVpreF recipients and infants of placebo recipients ranging from 10.9−13.6 at birth to 4.1−6.8 at 6 months of age, respectively (**Table S9**). These GMRs were similar regardless of maternal GA at vaccination (**Figure S3**). Estimated RSV-A and RSV-B neutralizing titer half-lives in infants were similar across RSVpreF groups, ranging from 40−45 days and 39−42 days, respectively; estimated half-life for combined RSV-A/-B neutralizing titers in infants was 39−44 days across RSVpreF groups. The maternal-to-infant placental transfer ratios of RSV-A, RSV-B, and RSV-A/-B combined neutralizing titers for RSVpreF were 1.35−1.77, 1.43−1.89, and 1.39−1.83, respectively (**Figure 4C; Figure S1C; Table S10**). The maternal-to-infant placental transfer ratios for placebo were 1.85, 1.71, and 1.78, respectively. Combined RSV-A/-B prefusion F binding IgG GMCs in infant participants and IgG maternal-to-infant placental transfer ratios showed a similar pattern to neutralizing GMTs (**Figure S2B−C**). Combined RSV neutralizing GMTs and anti-prefusion F IgG GMCs for maternal and infant participants are presented by hemisphere in **Table S11** and **S12**, respectively.

An exploratory analysis assessed VE of all RSVpreF vaccine groups combined versus placebo. Observed VE (95% CI) of RSVpreF against RSV-associated medically attended LRTI and medically attended severe LRTI in infants through 6 months of age was 75% (−11%, 94%) and 83% (−48%, 99%), respectively (**Table 2**). Observed VE from birth through 6 months of age was consistent with observed RSV neutralizing titers in infants, which remained above or comparable to protective titers associated with palivizumab (100-µg/mL serum concentration) and nirsevimab (6.8-µg/mL serum concentration; **Figure 4B**). Observed VE in infant participants by hemisphere is summarized in **Table S13**. However, small participant numbers particularly in the Southern Hemisphere limits interpretation of these endpoints by geographic subgroup.

DISCUSSION

RSV-associated illness in young infants is associated with high burden across countries and health systems [15-17]. Prevention of RSV illness through maternal vaccination is therefore a critical health priority to protect infants in the first months of life, a period of greatest vulnerability to adverse outcomes from RSV illness [18].

Results from the previous interim analysis of this global phase 2b study served as proof-of-concept, helping inform RSVpreF dose and formulation in the phase 3 MATISSE study in which efficacy against medically attended severe RSV-associated LRTI was confirmed [7,19]. In the planned interim analysis, RSVpreF at the 120-µg dose level without $Al(OH)_3$ was selected for further clinical investigation because neutralizing titers elicited by the 120-µg and 240-µg dose levels were similar, and although maternal neutralizing titers with an aluminum-containing formulation were somewhat higher, neutralizing titers in infants were higher in the formulation without aluminum [7]. The mechanism(s) behind the lack of an immunological benefit to the infant from the addition of aluminum to the maternal vaccine formulation are unclear. The aluminum adjuvant for the RSVpreF vaccine may not be required in antigen-experienced and immunologically primed individuals and addition of aluminum may not impact the transplacental transfer of RSV-specific antibodies.

In this final analysis of the phase 2b study, RSVpreF was generally safe, with findings consistent with that of the interim analysis, the pivotal phase 3 MATISSE efficacy trial, and postmarketing surveillance [7,19,20]. Most maternal participants had uncomplicated pregnancies and vaginal deliveries, most infants were born at term, and specific birth complications were reported with similar frequency across study groups. In this descriptive study, preterm birth was reported in approximately 5% of pregnancies in the RSVpreF groups and 3% in the placebo group without causal inference. A descriptive post hoc analysis of the MATISSE trial found no differences in preterm births between the RSVpreF and placebo groups [21]. Similarly, a retrospective cohort study of almost 3000 pregnant individuals conducted at 2 New York city hospitals found no evidence of increased risk of preterm birth [22]. Additionally, hypertensive disorders of pregnancy (pre-eclampsia/gestational hypertension) among maternal participants were uncommon and reported at similar frequencies across RSVpreF and placebo groups. This is consistent with findings from the phase 3 MATISSE efficacy study, in which maternal hypertensive disorders of pregnancy were observed in ≤1% of maternal RSVpreF or placebo recipients [7]. Data from real-world studies regarding risk of hypertensive disorders in pregnancy and receipt of RSVpreF are limited [23]. Therefore, the potential signals of preterm birth and hypertensive disorders of pregnancy should continue to be monitored [20].

Maternal vaccination with RSVpreF rapidly elicited robust RSV-A and RSV-B neutralizing antibody titers in maternal participants, with titers remaining well above baseline through 6 months after delivery. Maternal-to-infant placental antibody transfer was highly efficient. RSV neutralizing GMTs in infants through 6 months of life remained higher in those born to vaccinated

mothers than infants born to mothers who received placebo and did not vary substantially by maternal GA at vaccination, which is expected since most births were full-term. RSV-A/-B prefusion F binding IgG levels in maternal and infant participants showed a similar pattern to neutralizing titers, with highly efficient placental transfer. An exploratory efficacy analysis, while limited by the small number of observed cases of RSV-associated LRTI, suggested the transferred antibodies following RSVpreF vaccination were associated with prevention against medically attended RSV-associated LRTI in infants, a finding ultimately confirmed in appropriately powered pivotal phase 3 study analyses and supported by real-world analyses in a country implementing a national RSVpreF maternal vaccination program [19,24].

At the time of this study's interim analysis, we reported that infant cord blood serum neutralizing titers exceeded protective levels of the RSV monoclonal antibody prophylaxis, palivizumab [7]. Palivizumab at a dose providing a serum concentration of ~100 μg/mL is associated with protection of infants from hospitalization in the ICU for RSV-associated illnesses [7,11]. In this final analysis, which now includes data for both the Northern and Southern Hemispheres, we showed similar trends in these post hoc analyses, with infant RSV neutralizing titers remaining above or comparable to these protective thresholds through 6 months of age, both against palivizumab and the more recently licensed prefusion-F–specific nirsevimab. A nirsevimab serum concentration of 6.8 μg/mL is associated with 70% efficacy against medically attended RSV-associated LRTI in infants up to 5 months of age following mAb administration [12]. Potential advantages of maternal RSVpreF vaccination include the elicitation of polyclonal antibodies in contrast to administration of single-epitope monoclonal antibodies, for which effects on protection against mutant RSV strains have been described although their degree of clinical relevance continues to be assessed [25-27]. Additionally, RSV-B–resistant mutations have been reported for nirsevimab [28]. Notably, however, further real-world evidence will be important to better define potential differences in protective neutralizing antibody thresholds between RSV-A and RSV-B for nirsevimab.

A limitation of the current study is that pregnant individuals in the 24–27-week GA range were slightly underrepresented. The COVID-19 pandemic also affected enrollment and study execution at Southern Hemisphere sites, with less than half of planned maternal enrollment achieved, hampering comparisons of immune responses in different hemispheres. Restrictions associated with the COVID-19 pandemic also resulted in decreased circulation of RSV during the surveillance period, which affected exploratory efficacy assessments. Finally, data on long-term maternal antibody titers and potential implications for both maternal protection and future pregnancies were beyond the scope of this study but will be of interest in future investigations.

CONCLUSION

In conclusion, this final analysis of the RSVpreF phase 2b study confirms the findings of the interim analysis. RSVpreF vaccine had an acceptable safety profile in pregnant individuals and

their infants and elicited robust neutralizing antibody responses that were transplacentally transferred at levels associated with prevention of RSV-associated LRTI in infants in the first 6 months of life. These data supported selection of the non-aluminum-containing RSVpreF 120-µg formulation for further study in the pivotal phase 3 efficacy trial [19]. Licensure of RSVpreF 120 µg in 2023 and recommendation for maternal use in the United States and several other countries represent an important new step in preventing RSV illness in young infants.

FOOTNOTE PAGE

Data Availability Statement: 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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Conflict of Interest Disclosures: Eric A.F. Simões, Shabir A. Madhi, Alan T.N. Tita, Conrado Llapur, and José M. Novoa P. are Pfizer investigators. Kimberly J. Center, Kena A. Swanson, David Radley, Emily Gomme, Linda G. Brock, Daniel A. Scott, Iona Munjal, Stephanie B. McGrory, Annaliesa S. Anderson, William C. Gruber, and Alejandra C. Gurtman are current or former employees of Pfizer and may hold stock or stock options. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Contributors Statement: E.S., S.M., and J.N.P. were involved in data collection, formal analysis, investigation, and writing, reviewing and editing. K.C., D.S., I.M., S.McG., A.A., W.G., and A.G. were involved in conceptualization, study design, data collection, formal analysis, methodology, and writing, reviewing and editing. A.T. and C.L. were involved in data collection, investigation, and writing, reviewing and editing. K.S. was involved in conceptualization, study design, investigation, methodology, and writing, reviewing and editing. D.R. was involved in study design, data collection, formal analysis, methodology, and writing, reviewing and editing. E.G. and L.B. were involved in data collection, investigation, methodology, and writing, reviewing and editing. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Figure 1. Enrollment, randomization, and vaccine and placebo administration for maternal participants. NH, Northern Hemisphere; SH, Southern Hemisphere.

ALT TEXT. Disposition flow chart for maternal participants

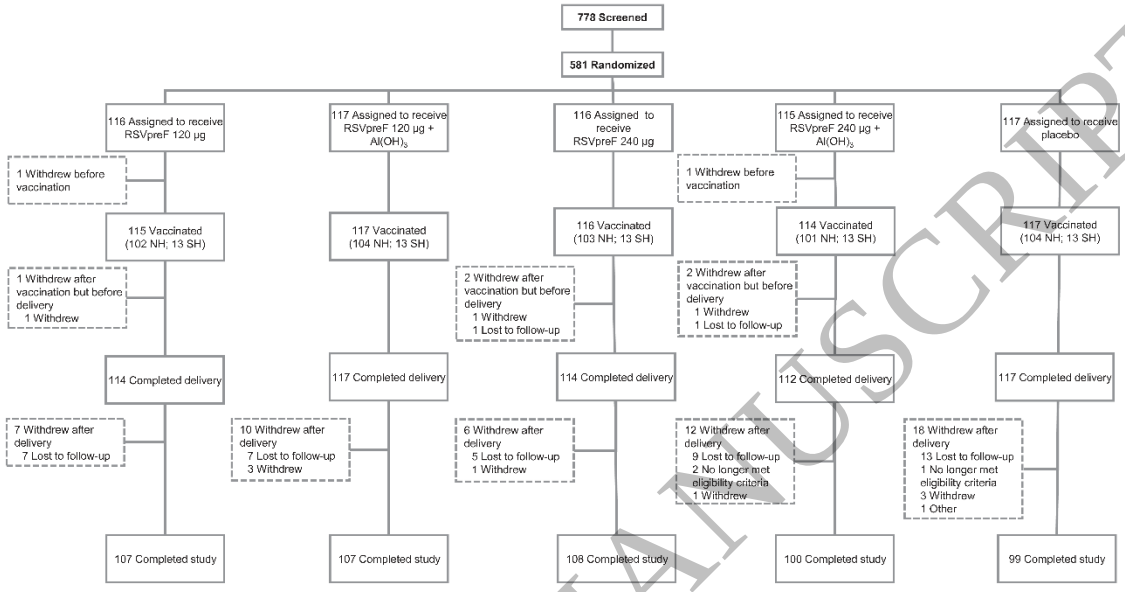

Figure 2. Disposition for infant participants by vaccine group of their mother.

ALT TEXT. Disposition flow chart for infant participants

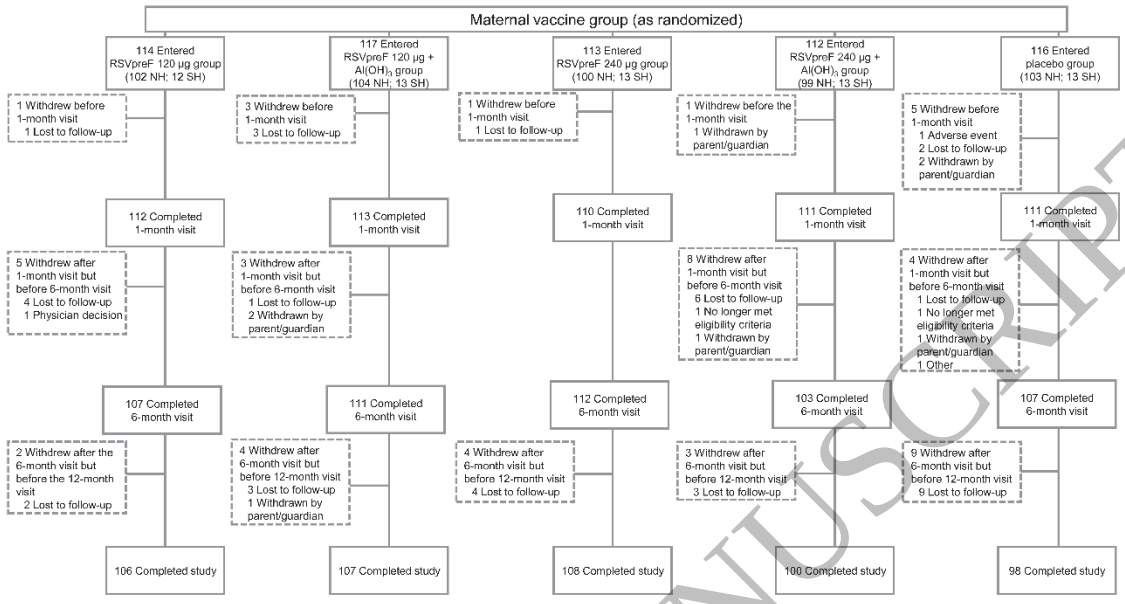

Figure 3. AEs occurring (A) 1 month after vaccination in maternal participants and (B) in the first 1 month of life in infant participants (safety population). AEs were categorized according to *Medical Dictionary for Regulatory Activities* version 24.1 terms. The numbers above the bars are the percentage of participants. [a]As assessed by the investigator (dizziness occurring in 1 maternal participant in the RSVpreF 120-µg group).

ALT TEXT. Bar graph summarizing adverse events in maternal and infant participants

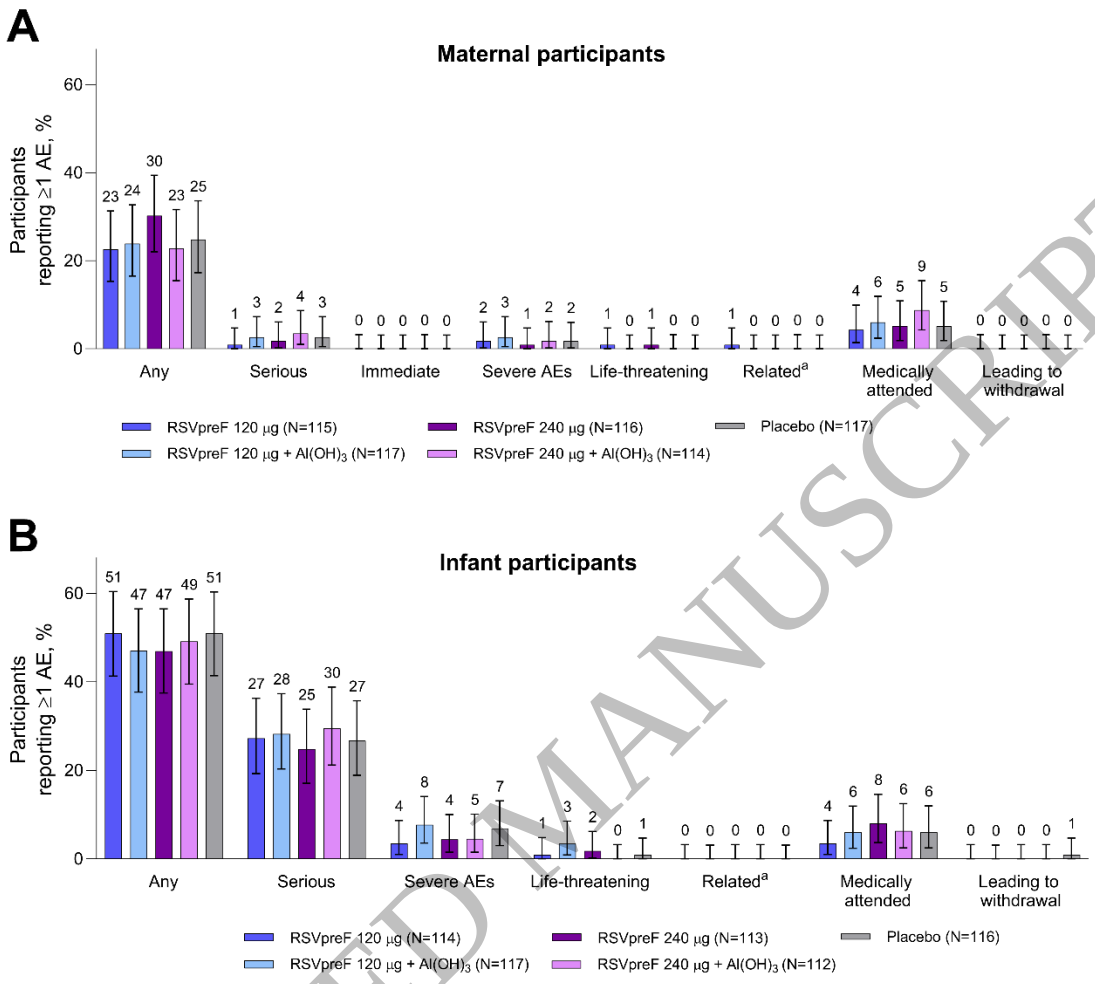

Figure 4. RSV-A and RSV-B 50% neutralizing titers (NT50) among (A) maternal participants and (B) infant participants, and (C) maternal-to-infant placental transfer ratio of RSV NT50 at delivery for maternal participants and birth for infant participants in the evaluable immunogenicity population presented using a $\log_{10}$ scale. Gray broken lines represent the assay lower limit of quantitation. Palivizumab (green) and nirsevimab (blue) reference lines corresponding to RSV NT50 values conferring 90% protection are shown (neutralizing titer at ~100-µg/mL and ~6.8-µg/mL serum concentration, respectively). In (C), maternal-to-infant transfer ratios are RSV-neutralizing titers for each mother–infant pair.

ALT TEXT. Line graphs showing RSV-A and RSV-B 50% neutralizing titers over time in maternal and infant participants, and bar graphs showing transplacental transfer ratios of antibodies.

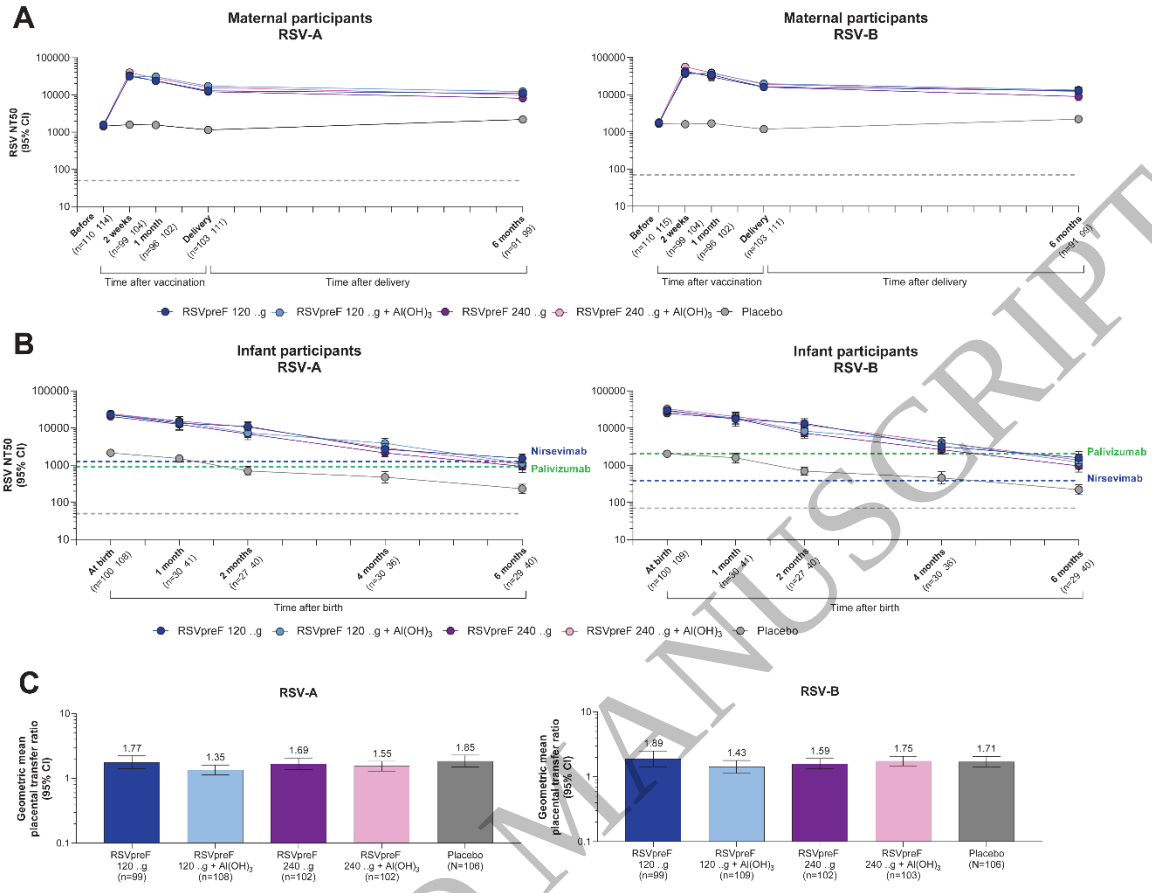

Table 1. Birth Outcomes and Congenital Abnormalities in Infant Participants

Outcome	Study Group (as Administered)				
	RSVpreF 120 µg	RSVpreF 120 µg + Al(OH)$_3$	RSVpreF 240 µg	RSVpreF 240 µg + Al(OH)$_3$	Placebo
GA, weeks					
N[a]	114	117	113	112	116
Mean (SD)	39.06 (1.09)	38.96 (1.28)	38.86 (1.52)	39.07 (1.09)	39.08 (1.17)
Median (range)	39.14 (35.4–41.4)	39.00 (31.4–41.0)	39.00 (31.3–41.6)	39.29 (34.7–41.4)	39.14 (33.1–41.7)
Prematurity, n (%)	6 (5)	4 (3)	8 (7)	4 (4)	3 (3)
Congenital malformation/anomaly[b], n (%)	19 (17)	14 (12)	16 (14)	22 (20)	16 (14)
Congenital abnormality[c], n (%)					

N[a]	114	117	113	112	116
Any	11 (10)	5 (4)	2 (2)	2 (2)	7 (6)
Cardiac disorders	2 (2)	0	0	0	0
Mitral valve incompetence	1 (1)	0	0	0	0
Pulmonary valve stenosis	1 (1)	0	0	0	0
Congenital, familial, and genetic disorders	10 (9)	5 (4)	2 (2)	2 (2)	6 (5)
Alpers disease	0	1 (1)	0	0	0
Ankyloglossia congenital	3 (3)	0	0	1 (1)	1 (1)
Aplasia cutis congenita	0	0	0	0	1 (1)
Atrial septal defect	2 (2)	1 (1)	0	0	1 (1)
Chordee	1 (1)	0	0	0	0
Chromosomal deletion	1 (1)	0	0	0	0
Cleft lip	1 (1)	0	0	0	0
Cleft palate	1 (1)	0	0	0	0
Cryptorchism	1 (1)	0	0	0	1 (1)
Cystic fibrosis	1 (1)	0	0	0	0
Dacryostenosis congenital	0	0	1 (1)	0	0
Hydrocele	1 (1)	1 (1)	0	0	1 (1)
Hypospadias	1 (1)	0	1 (1)	0	0
Labial tie	0	0	0	0	1 (1)
Laryngomalacia	0	1 (1)	0	0	0
Patent ductus arteriosus	2 (2)	0	0	0	1 (1)
Penile torsion	0	0	0	1 (1)	0
Spina bifida cystica	0	1 (1)	0	0	0
Ventricular septal defect	1 (1)	0	0	0	0
Gastrointestinal disorders	0	0	0	0	1 (1)
Umbilical hernia	0	0	0	0	1 (1)
Neoplasms benign, malignant, and	0	1 (1)	0	0	0

unspecified (including cysts and polyps)					
Hemangioma of skin	0	1 (1)	0	0	0

Data are for the safety population.
[a]Number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
[b]As indicated in the case report form.
[c]Of at least moderate severity and as reported throughout the study (by system organ class and preferred term according to the *Medical Dictionary for Regulatory Activities* version 24.1).

Table 2. Observed Efficacy of Maternal RSVpreF Vaccination Against RSV-Associated LRTI in infants

	Maternal Study Group (as Administered)		
Endpoint	RSVpreF (N[a]=456) n (%)	Placebo (N[a]=116) n (%)	VE[b] % (95% CI)
Medically attended LRTI[c]	5 (1.1)	5 (4.3)	75 (–11, 94)
Medically attended severe LRTI[d]	2 (0.4)	3 (2.6)	83 (–48, 99)

SpO_2, peripheral capillary oxygen saturation.
Medically attended visit describes when an infant participant has been taken to or seen by a healthcare provider (eg, outpatient or inpatient visit, emergency room, urgent care, or home visit).
All 95% CIs for VE include zero.
[a]Number of participants (at risk) in the specified group. These values are used as the denominators for the percentage calculations.
[b]VE was calculated as 1-(hP/[1-P]), where P is the number of RSVpreF cases divided by the total number of cases and h is the ratio of number of participants at risk in the placebo group to the number of participants at risk in the RSVpreF group.
[c]Defined as a medically attended visit and presence of 1 of the following signs of LRTI: tachypnea (respiratory rate ≥60 breaths per minute [<2 months (60 days) of age] or ≥50 breaths per minute [≥2 to 12 months of age]); SpO_2 measured in room air <95%; chest wall indrawing.
[d]Defined as a medically attended visit and presence of 1 of the following signs of severe LRTI: tachypnea (respiratory rate ≥70 breaths per minute [<2 months (60 days) of age] or ≥60 breaths per minute [2–12 months of age]); SpO_2 measured in room air <93%; high-flow nasal cannula or mechanical ventilation (invasive or noninvasive); ICU admission for >4 hours; unresponsive/unconscious.