Maternal/Pediatric RSV Work Group Considerations

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Outline

- Anticipated supply of maternal RSV vaccine and nirsevimab
- Updates on post-introduction nirsevimab and maternal RSV vaccine safety and effectiveness monitoring
- Revaccination of pregnant people during subsequent pregnancies

Anticipated supply of maternal RSV vaccine and nirsevimab for 2024–2025 RSV season

- For maternal RSV vaccine, no anticipated supply/demand mismatch
- For nirsevimab, limited availability beginning early September, ramping up during September, broadly available by October 1
- Original ACIP recommendations (as published in MMWR) apply for 2024-25 RSV season
- All infants are recommended to be protected by either maternal RSV vaccination or nirsevimab for the 2024-25 RSV season

Updates on post-introduction nirsevimab and maternal RSV vaccine safety and effectiveness monitoring

Maternal RSV vaccine safety

- **Among reports received in VAERS after maternal Pfizer RSV vaccine, the most frequent adverse events reported were local and systemic symptoms (e.g., headache) and pregnancy specific conditions (e.g., preterm delivery)**
  - Expected for a vaccine recommended for pregnant persons at 32-36 weeks' gestation
  - No verified reports of Guillain Barré syndrome
- **Preliminary findings in the Vaccine Safety Datalink (VSD) suggest that the incidence of preterm births is 4.1% among pregnant persons who received Pfizer RSV vaccine during the 2023-2024 respiratory season**
  - Within VSD's expected historical range of the incidence of preterm births at 32-36 weeks' gestation (3.1–6.1%) before introduction of this vaccine
  - Matched analysis for preterm birth and other safety outcomes is in progress

The Vaccine Adverse Event Reporting System (VAERS)
Vaccine Safety Datalink (VSD) | CDC

Nirsevimab adverse event reporting

- **Suspected adverse reactions after nirsevimab administration are recommended to be reported to MedWatch**
  - These reports are entered into the FDA Adverse Event Reporting System (FAERS) database
- **If administered on the same day as a vaccine, suspected adverse reactions after nirsevimab are reported to VAERS**
  - FDA/CDER reviewers review these VAERS reports
- **Similar to VAERS, an incidence of an adverse event cannot be determined from voluntary reporting**

FDA Adverse Event Reporting System (FAERS) Public Dashboard | FDA

Summary of nirsevimab post-marketing adverse events reported to FAERS and VAERS

- **The most frequently reported adverse events involved patients who reportedly developed breakthrough RSV infections despite receiving nirsevimab, and included signs, symptoms, or complications of these infections (e.g., bronchiolitis)**
- **Cases of serious hypersensitivity reactions with nirsevimab were identified in the post-marketing setting and the product labeling was updated in February 2024**
  - *Serious hypersensitivity reactions have been reported following BEYFORTUS administration. These reactions included urticaria, dyspnea, cyanosis, and/or hypotonia.*
- **No additional safety signals have been identified at this time**

FDA Adverse Event Reporting System (FAERS) Public Dashboard | FDA

WG considerations on safety

- Safety data on nirsevimab and maternal RSV vaccine are reassuring, but population-based studies with comparison groups are needed and pending
- Because of U.S. recommendation that Pfizer maternal RSV vaccine be given at 32–36 weeks gestation, unlikely to accumulate U.S. data on safety of vaccine given at 24–31 weeks gestation
- Hypersensitivity reactions in young infants are rare and can be difficult to discern from startle reactions or vasovagal reactions[1]

[1] Agrabenhenrich et al. 2016 J Allergy Clin Immunol

Nirsevimab effectiveness

- **Effectiveness against RSV-associated hospitalization was 91% in NVSN and 98% in VISION**
- **Effectiveness against any medically attended RSV-associated ARI episode in NVSN was 89%, and effectiveness against RSV-associated ED visits was 77% in VISION**
- **CDC platform estimates are consistent with studies in Europe,[1]**
- **Longer follow up time needed to determine duration of protection**
- **Limited impact on RSV hospitalization burden, likely because of late administration**
  - Substantial decreases in RSV-associated hospitalizations in young infants reported in Spain, Luxembourg, and Italy with early implementation and high coverage[2]

[1] Consolati Vaccine 2024; Ezpeleta Vaccine 2024; Lopez-Lacort Eurosurveillance 2024; Ares-Gomez Lancet Inf Dis 2024; Coma SSRN preprint 2024;
[2] Ernst Eurosurveillance 2024; Consolati Vaccine 2024; Mazagatos Influenza Other Respir Viruses 2024

Maternal RSV vaccine effectiveness

- **Unable to estimate maternal RSV vaccine effectiveness during the 2023-24 season due to**
  - Limited uptake of maternal RSV vaccine
  - Early onset of the 2023-2024 RSV season
  - Timing of vaccine rollout

- **CDC will continue to monitor maternal RSV vaccine effectiveness in future seasons**

WG considerations on effectiveness

- **Evidence shows nirsevimab to be highly effective**
- **Duration of protection from nirsevimab and maternal vaccination remains unknown**
- **Important studies are needed for 2024-25 season and future RSV seasons**
  - Maternal vaccine effectiveness
  - Nirsevimab effectiveness with longer follow up time, which should be available with earlier widespread availability
  - Nirsevimab effectiveness among children aged 8–19 months with increased risk for severe disease during their second RSV season
  - Impact on RSV burden when nirsevimab and maternal vaccine are given with earlier administration and potentially increased uptake

Revaccination of pregnant people during subsequent pregnancies

Additional RSV vaccine doses in subsequent pregnancies

- **ACIP recommendations for Pfizer RSV maternal vaccine state that**
  - *Currently, no data are available on either the efficacy of the first lifetime dose to protect infants born after subsequent pregnancies or the safety of additional doses given during subsequent pregnancies. Additional data are needed to determine whether additional seasonal doses during subsequent pregnancies are indicated, and ACIP might update recommendations in the future, as data become available.*
- **Still no data on additional RSV vaccine doses in subsequent pregnancies**
- **There are potentially people who received an RSV vaccine during pregnancy for the 2023-24 RSV season who could have a subsequent pregnancy during the 2024-2025 RSV season**

Pfizer ABRSYSVO vaccine efficacy against primary clinical trial outcomes over time among adults aged ≥60 years

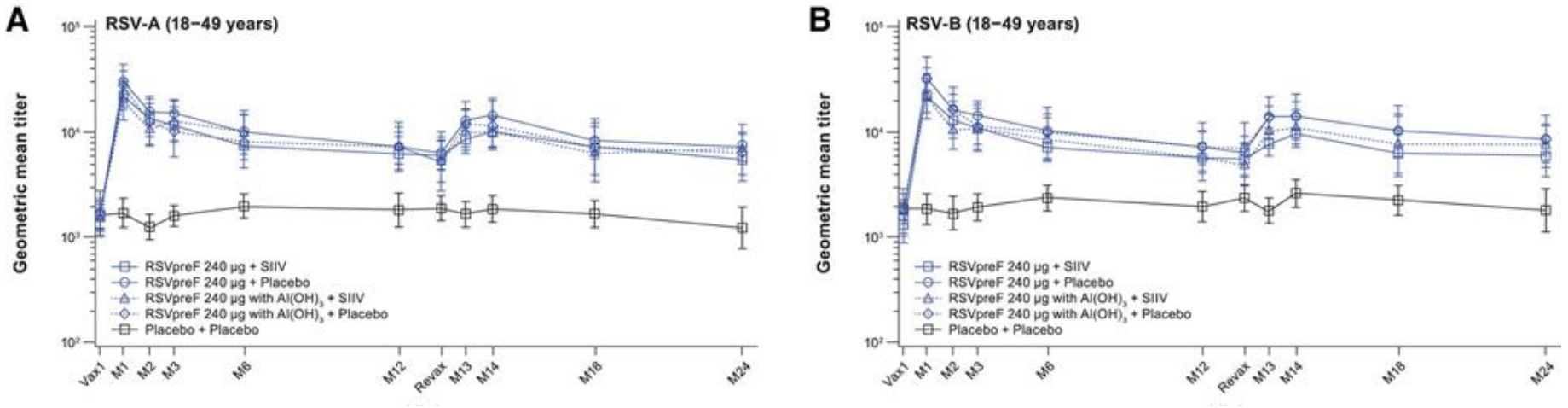
Vaccine	Primary outcome	Efficacy (95% CI), months 0–12[a]	Efficacy (95% CI), months 13–24[a]
Pfizer ABRYSVO	RSV LRTI with ≥2 lower respiratory sx	**62%** (41, 76) Median **12** months follow-up per participant	**55%** (26, 73) Median **6** months follow-up per participant
	RSV LRTI with ≥3 lower respiratory sx	**86%** (63, 96) Median **12** months follow-up per participant	**74%** (27, 92) Median **6** months follow-up per participant

Abbreviations: CI: confidence interval, LRTI: lower respiratory tract illness, sx: signs or symptoms, LRTD: lower respiratory tract disease

a. Nominal 12-month efficacy. Not all trial participants contributing to each estimate had 12 months' follow up time. Median per-participant follow-up time is reported below each estimate.

Pfizer RSV vaccine Phase 1/2 immunogenicity results in nonpregnant adults

- **Antibody titer lower following 2nd dose at 12 months than initial response**
- **Antibody titer prior to 2nd dose above baseline**



J Infect Dis, jiae185, https://doi.org/10.1093/infdis/jiae185

Tdap recommended during each pregnancy

- **ACIP Tdap recommendations state that "When ACIP considered recommending Tdap vaccination during each pregnancy, the safety information concerning booster doses of Tdap in pregnant women previously vaccinated with Tdap was not available"**
- **"ACIP recognized the need for safety studies of severe adverse events when Tdap is administered during subsequent pregnancies but concluded that the potential benefit of preventing pertussis morbidity and mortality in infants too young to be fully vaccinated outweighs the theoretical concern of possible localized severe adverse events in pregnant women receiving Tdap. ACIP also concluded that experience with tetanus toxoid–containing vaccines suggests no excess risk for severe adverse events among women receiving Tdap with each pregnancy."**

Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) | MMWR (cdc.gov)

Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccine (Tdap) in Pregnant Women — Advisory Committee on Immunization Practices (ACIP), 2012 (cdc.gov)

WG consideration on additional RSV vaccine doses in subsequent pregnancies

- **Concerning that data in older adults suggest revaccination does not restore antibody levels to those after first dose**
  - Antibody levels are particularly important for maternal vaccination since infants are protected through transplacental transfer of antibodies
- **RSV vaccine differs from Tdap vaccine**
  - Maternal RSV vaccine has a potential safety concern for preterm birth and hypertensive disorders of pregnancy
  - Alternative product, nirsevimab, exists that can protect infants from severe RSV for subsequent pregnancies

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

WG considerations for needed data to make RSV vaccine recommendations during subsequent pregnancies

- **Additional data are needed prior to recommending RSV vaccine during each pregnancy (i.e., during subsequent pregnancies)**
  - Antibody data in pregnant people and infants with vaccination during subsequent pregnancies
  - Safety data (e.g., reactogenicity) with vaccination during subsequent pregnancies
  - Safety data of RSV vaccine during the first pregnancy it is administered, particularly regarding outcomes of preterm birth and hypertensive disorders of pregnancy

Recommendations for additional RSV vaccine doses in subsequent pregnancies

- **People who received a maternal RSV vaccine during a previous pregnancy are not recommended to receive additional doses during future pregnancies**
- **Infants born to people who were vaccinated only during a prior pregnancy should receive nirsevimab**
- **Recommendations can be updated in the future if additional data are available**

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 cdc.gov