Clinical considerations for RSVpreF maternal vaccine and nirsevimab

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Policy questions for ACIP vote

- Should vaccination with Pfizer RSVPreF vaccine (120µg antigen, 1 dose IM given 24-36 weeks gestation) be recommended for pregnant people to prevent RSV disease in infants?
- Should one dose of nirsevimab be recommended for infants born during or entering their first RSV season and <8 months of age at time of immunization?
- Should one dose of nirsevimab be recommended for children who are at increased risk of severe RSV disease entering their second RSV season and <20 months of age at time of immunization?

Potential advantages of maternal vaccination versus a monoclonal antibody (mAb)

- A maternal vaccine may be lower in price
- A mAb is not a traditional vaccine and many issues may complicate implementation
  - Insurance coverage, vaccine schedule, immunization registries, safety monitoring
- Maternal vaccine provides protection from birth, when infants are at highest risk
  - A mAb must be timed correctly to provide protection during the RSV season, and atypical RSV transmission may lead to unprotected infants
- Maternal vaccine induces a polyclonal antibody response, which should be more resilient to mutations than a monoclonal antibody
  - Evidence suggests that mutations resulting in nirsevimab resistance are rare, but naturally occurring resistant mutations have been detected[1,2]
  - Mutations resulted in poor efficacy of a previous mAb product (suptavumab)[3]

[1] Abram IDweek 2022. [2] Abram 12th RSV International Symposium 2022. [3] Simões CID 2021.

Potential advantages of mAb over maternal vaccination

- Imbalance for preterm birth observed after RSVpreF vaccine vs. placebo in maternal clinical trials, but not statistically significant[1]
- No head-to-head trials comparing efficacy, but protection from maternal vaccination likely wanes more quickly[1–4]
- Estimated half-life in nirsevimab trials
  - Nirsevimab: 63–73 days[5,6]
  - Infection-induced maternal RSV antibodies: 36–38 days[5]
- Nirsevimab administration can be timed to be given when infant is entering RSV season

[1] Kampmann NEJM 2023. [2] Muller NEJM 2023. [3] Madhi NEJM 2020. [4] Nunes F1000Res 2018. [5] Wilkins Nat Med 2023. [6] Griffin NEJM 2020.

Potential advantages of mAb over maternal vaccination (continued)

- Protection from maternal vaccination relies on sufficient transplacental transfer of antibodies, which may be reduced in
  - Infants born soon after maternal immunization[1]
  - Infants born premature[2]
  - Maternal disease[2]
- Maternal uptake of flu and Tdap vaccines lower than routine childhood vaccines[3,4]
  - Unclear if pregnant people willing to accept multiple vaccines during pregnancy
  - However, flu vaccine uptake among children only mildly higher than among pregnant people
  - Uptake of maternal RSVpreF vaccine and nirsevimab unknown

[1] https://www.cdc.gov/vaccines/pregnancy/vacc-during-after.html. [2] Palmerira Clin Dev Immunol 2012.
[3]https://www.cdc.gov/flu/fluvaxview/pregnant-women-apr2022.htm. [4] Hill MMWR 2023

Benefits of both products being available

- Each product has certain advantages
- Parental preferences may differ, as suggested by survey asking pregnant people about product preference if both available[1]
  - 28% only maternal vaccine
  - 25% only RSV antibody injection
  - 38% both
  - 8% none
  - 1% other
- Some populations lack access or do not present for prenatal care, precluding maternal vaccination
- Scenarios may exist for which use of both products may be warranted to maximize protection from RSV-associated severe disease

[1] Unpublished CDC and University of Iowa/RAND survey of 523 people currently pregnant or pregnant within last 12 months of survey conducted December 21, 2022-January 2, 2023

Cost effectiveness summary

- Cost effectiveness of giving nirsevimab if mother had been vaccinated
  - $668,735/QALY if given to all infants
  - $486,882/QALY if given to infants born April to September

- Cost effectiveness of giving RSVpreF to mother if nirsevimab will be given
  - More than $10,000,000/QALY on average

Challenges if nirsevimab recommendations relate to maternal vaccination status

- Maternal vaccination status might be unknown

- Transferring documentation of maternal vaccination to the healthcare provider of infant may be difficult
  - Limited information available during birth hospitalization
  - Less information regarding receipt of prenatal vaccinations may be available to infant primary care providers

Draft clinical considerations if both RSVpreF and nirsevimab are licensed and recommended

- Either maternal vaccination with RSVpreF or nirsevimab is recommended to prevent RSV disease, but both products are not needed for most infants
- Risks and benefits of both RSVpreF and nirsevimab should be considered when deciding on maternal vaccination
- If mother vaccinated, nirsevimab can be considered if infant considered to have insufficient protection from vaccine or is at high risk of severe disease

Scenarios to consider administration of nirsevimab when mother has been vaccinated

- Receipt of maternal vaccine not confirmed by healthcare record
- Infant born within 14 days of vaccination
- Infant born premature
- Healthcare provider recommends maximizing protection because infant at high risk of severe disease
  - Especially important if born >3 months prior to peak of RSV season

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

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