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Modeled head-to-head comparison of nirsevimab and RSVpreF maternal vaccine in the US

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BACKGROUND

- Respiratory syncytial virus (RSV) is the leading cause of hospitalizations in all infants in North America and imposes a substantial burden on ambulatory care settings. Most hospitalizations due to RSV (~67% to 87%) occur in healthy infants born at term, and between 45% and 66% of infants admitted to the ICU due to RSV are previously healthy.[1-5]
- Nirsevimab is the first monoclonal antibody approved for the prevention of RSV in all infants through their first RSV season. RSVpreF, a bivalent RSV prefusion F protein–based has been approved for the prevention of RSV in infants through active immunization of pregnant individuals 32-36 weeks of gestational age (wGA).

OBJECTIVES

- To analyze and compare the impact of new preventative products for the prevention of RSV lower respiratory tract diseases (LRTD) in the US birth cohort over the first RSV season of the infants' life,
  - To estimate the protection offered by nirsevimab in terms of number of events avoided during the first RSV season of infants' life, compared to standard of practice (SoP),
  - To estimate the protection offered by RSVpreF vaccine in terms of number of events avoided during the first RSV season of infants' life, compared to SoP.

METHODS

- **Static decision analytic model** to estimate health, cost and quality-of-life outcomes related to RSV in children, with or without immunization[6]
- **The target population** includes 3 groups, reflecting the level of individual risks of LRTD:
  - **Palivizumab-eligible** infants per the latest AAP recommendations.[7]
  - **Preterm** infants include infants born between 29 wGA and 34 weeks, six days of gestational age (not eligible for immunization with palivizumab).
  - **Term and late preterm** infants include infants born at or after 35 wGA (not eligible for immunization with palivizumab).
- **Intervention strategy**
  - **Comparative strategy – Standard of Practice**: monthly administrations of palivizumab during the RSV season for palivizumab-eligible infants only (with a maximum of five doses), as per the AAP recommendations,[7] and no prophylaxis for the preterm and term infant populations.
  - **Intervention strategy – "nirsevimab"**: Immunization with nirsevimab for the entire birth cohort.
  - **Intervention strategy – "RSVpreF"**: Year-round immunization of pregnant individuals 32-36 wGA with the RSVpreF vaccine.
- **The RSV season** modeled in the base case assumes virus circulation from October through March, a peak in December - January and low RSV circulation between April and September.[8]
- **Inputs** were obtained from literature and are presented in **Table 1**

Table 1: Inputs

	Palivizumab-eligible Population	Preterm infants (<35wGA)	Late preterm and term infants (≥35 wGA)
Demographics			
Size of the US birth Cohort	1.58% (57,907)[9-10]	4.22% (154,663)[9,11]	94.20% (3,452,430)[11]
Event rates			
Hospitalizations[1-2,8,12-14]			
0-11 months	8.85%	2.23%	1.20% (0.84% - 2.6%)
ICU admission*	29.25%	31.25	22% (10% - 35.5%)
ICU with MV*	8%	10.25%	3.75%
Emergency room (ER) visits[9,15]			
0-11 months	6.62% (5.66% - 7.57%)		
% of LRTD	57.5%		
Primary care (PC) visits[9,15]			
0-11 months	23.09% (19.25% - 26.93%)		
% of LRTD	47.5%		
RSV related mortality (per 100,000)[16]			
0-11 months	2.4 (1.2 – 2.9)		

Abbreviations: RSV = respiratory syncytial virus ; LRTD = lower respiratory tract disease ; wGA = week of gestational age ; NA = Not applicable
*Conditional to hospitalization

- **The efficacy of nirsevimab** is sourced from MEDLEY, Ph2b, MELODY and HARMONIE trials. We assumed a non-inferiority between palivizumab and nirsevimab.
- **The efficacy of RSVpreF** is based on MATISSE results and FDA analysis over time. RSVpreF is assumed to not replace palivizumab in the eligible population, and efficacy in preterm infants is adjusted given the week of gestational age.
- We applied a similar methodology as in Hutton et al.[8] for both products where:
  - the hospitalization endpoints were applied on inpatient events,
  - RSV MALRTD endpoints were applied for the outpatient settings (i.e., ER and PC).

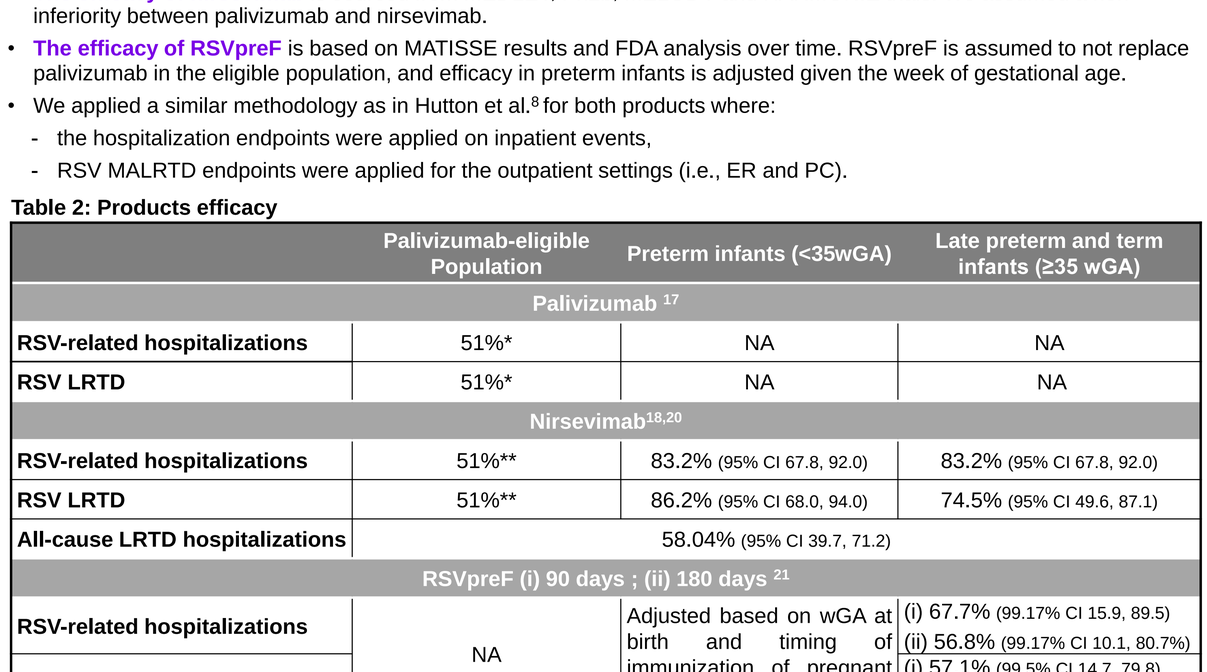
Table 2: Products efficacy

	Palivizumab-eligible Population	Preterm infants (<35wGA)	Late preterm and term infants (≥35 wGA)
Palivizumab [17]			
RSV-related hospitalizations	51%*	NA	NA
RSV LRTD	51%*	NA	NA
Nirsevimab[18,20]			
RSV-related hospitalizations	51%**	83.2% (95% CI 67.8, 92.0)	83.2% (95% CI 67.8, 92.0)
RSV LRTD	51%**	86.2% (95% CI 68.0, 94.0)	74.5% (95% CI 49.6, 87.1)
All-cause LRTD hospitalizations	58.04% (95% CI 39.7, 71.2)		
RSVpreF (i) 90 days ; (ii) 180 days [21]			
RSV-related hospitalizations	NA	Adjusted based on wGA at birth and timing of immunization of pregnant individuals	(i) 67.7% (99.17% CI 15.9, 89.5) (ii) 56.8% (99.17% CI 10.1, 80.7%)
RSV LRTD			(i) 57.1% (99.5% CI 14.7, 79.8) (ii) 51.3% (97.58% CI 29.4, 66.8)
All-cause LRTD hospitalizations	NA		

Abbreviations: LRTD = lower respiratory tract disease ; wGA = week of gestational age ; NA = Not applicable
*Efficacy applied prior to the introduction of palivizumab. **Nirsevimab efficacy for the palivizumab-eligible population is assumed to be non-inferior to that of palivizumab in the same population

- **The duration of protection** is set to 30 days for palivizumab, 150 days for nirsevimab, with a sustained protection over time, and 180 days for RSVpreF, with a decay of protection, based on efficacy per time interval. At the end of protection of the respective prophylaxes, the model applied an "on-off" strategy, meaning the protection drops to 0%. The **Figure 1** illustrates the protection over time for nirsevimab and RSVpreF considered in the model, using the example of RSV LRTD efficacies in term infants. The shape of decay for RSVpreF is the same for the hospitalization endpoint.

Figure 1: Modelled efficacy of nirsevimab and RSVpreF over time, example of RSV LRTD efficacy in term infants

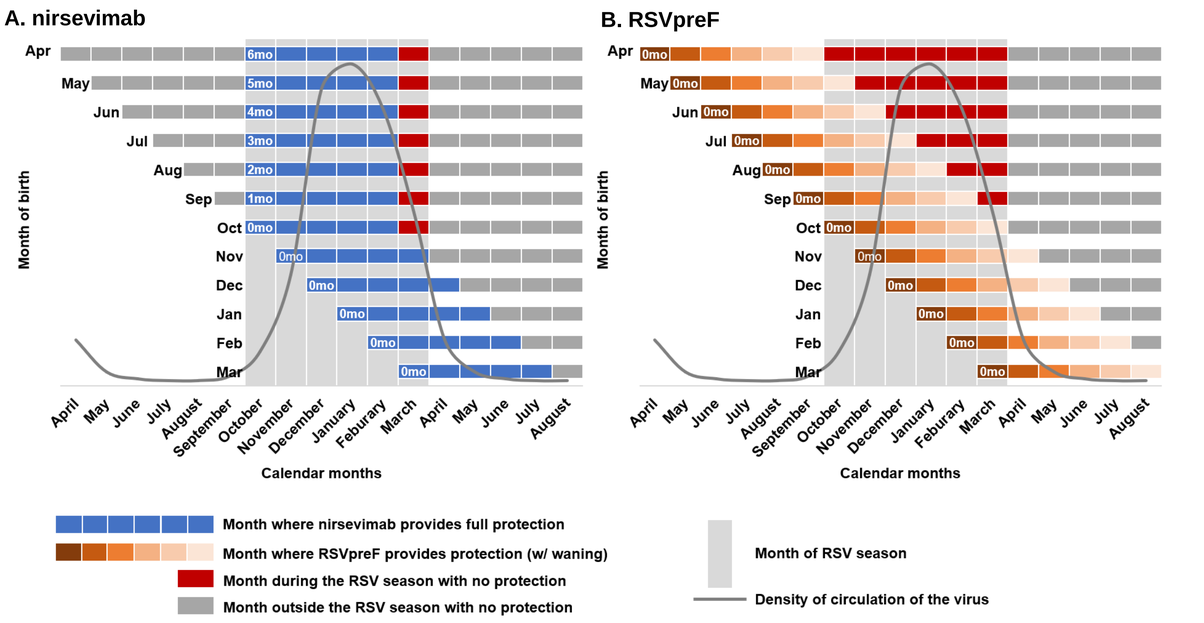


Abbreviations: RSV = respiratory syncytial virus; LRTD = lower respiratory tract disease

IMPLEMENTATION AND COVERAGE RATE

- **Implementation**:
  - **Nirsevimab** is implemented on a seasonal basis, with administration in October for infants born before the RSV season (Apr – Sep), and a dose at birth for infants born during the season (Oct-Mar) (**Figure 2A**).
  - **RSVpreF** is given year-round to pregnant individuals, with a protection offered to infants from birth through 6 months of age (**Figure 2B**).
- **Coverage rate**
  - **Nirsevimab**: the coverage rate is based on uptake of DTP pediatric vaccine at 80.4%.[22]
  - **RSVpreF**: for sake of comparison of the main results, we assumed similar coverage rate between nirsevimab and RSVpreF (80.4%). We tested also a coverage rate at 50%, in line with current recommended maternal vaccines.

Figure 2. Protection provided by nirsevimab and RSVpreF per month of birth and calendar months.

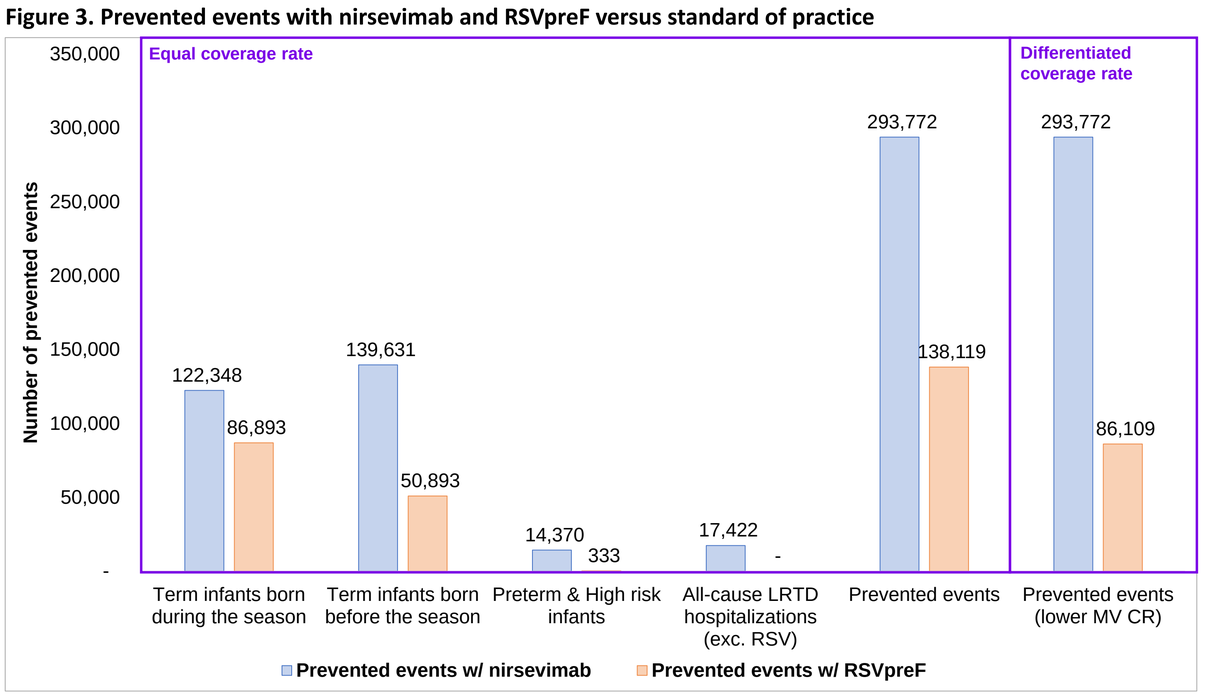


Abbreviations: RSV = respiratory syncytial virus

RESULTS

- **Equal coverage rate**
  - A total of 293,772 events could be prevented with nirsevimab, while MV, with the same coverage rate (80.4%), could prevent about half as many events (138,119).
  - The differential (**Figure 3**) can be attributed to the following features of nirsevimab, lacking for MV:
    - (i) the constant efficacy over time versus decay of maternal protection,
    - (ii) a timely immunization when RSV circulates,
    - (iii) the protection of all infants regardless of gestational age,
    - (iv) the significant protection against all-cause LRTD hospitalizations.
- **Differentiated coverage rate**
  - Given existing recommendations for 3 other vaccinations during pregnancy (Tdap, influenza, and COVID) and current uptake levels of these vaccines, results are also shown for a lower coverage rate (50%), which results in a fewer number of events averted (86,109) (**Figure 3**).

Figure 3. Prevented events with nirsevimab and RSVpreF versus standard of practice



Abbreviations: RSV = respiratory syncytial virus ; LRTD = lower respiratory tract disease ; MV = maternal vaccine ; CR = coverage rate

CONCLUSIONS

• No head-to-head trial has been performed to assess nirsevimab versus RSVpreF vaccine, and endpoints from the different clinical programs are not strictly comparable. However, the impact of nirsevimab and RSVpreF can be estimated versus the standard of practice, and still compared, considering both products are designed to prevent the same disease in the same target population.

• In this model, nirsevimab is estimated to prevent twice more cases than RSVpreF, at an equal coverage rate.

• Applying a more realistic coverage rate for the maternal vaccine, nirsevimab can prevent as many as 3 times more cases than RSVpreF.

• This difference is due to unique features of maintained efficacy through a typical RSV season, timely immunization, ability to protect regardless of the gestational age, and significant protection against all-cause LRTDs.

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CONFLICTS OF INTEREST:
AK, MG, EH, CF, MG, CR, JL, CR, and MT: Sanofi employees, may hold stock and/or stock options in the company.
KB: AstraZeneca employee, may hold stock and/or stock options in the company.

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