

Effectiveness of Nirsevimab Against RSV and RSV-Related Events in Infants

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INTRODUCTION

- Respiratory syncytial virus (RSV) has been the leading cause of LRTD in infants, nearly all children are infected by 2 years of age. About 40% of infected population develops LRTD, predominantly presenting as bronchiolitis or pneumonia
- All infants, including those born at full-term, are at risk for severe RSV with LRTD, which constitutes the leading cause of hospitalization in infants younger than 1 year
- Nirsevimab, a long-acting monoclonal antibody was approved by FDA in 2023, and recommended by ACIP for the prevention of RSV-associated LRTD in infants as well as older children at higher-risk for RSV disease^{1,2}



OBJECTIVE

- To assess the real-world effectiveness of nirsevimab against PCR-confirmed RSV LRTD and RSV-associated healthcare utilization in healthy term infants



METHODS

STUDY DESIGN

- Retrospective cohort study
- Included healthy infants born between April 1, 2023 and April 30, 2024 at KPNC
 - KPNC is an integrated healthcare delivery system with annual membership of approximately 4.6 million and an annual birth cohort of approximately 40,000 infants. KPNC members comprise approximately one-third of Northern California's population
- Routine nirsevimab administration and observation began on October 19, 2023, or date of birth, whichever was later

PARTICIPANTS

Inclusion Criteria

- Healthy infants born at KPNC, at a gestational age of ≥ 37 weeks, without any high-risk diagnosis that would increase risk of RSV whose mothers received prenatal care at KPNC to ascertain maternal RSV vaccination status

Exclusion Criteria

- Preterm infants or infants with pre-existing medical conditions
- Whose mothers received maternal RSV vaccination
- Infants with a record of positive RSV PCR test prior to October 19, 2023



OUTCOMES

Primary endpoint

- First episode[†] of PCR-confirmed RSV infection with an LRTD diagnosis

Coprimary endpoint

- Number of healthcare visits associated with an RSV LRTD episode

Secondary endpoint

- Any PCR-confirmed RSV (with or without the diagnosis of LRTD)

Post-hoc Analyses

- Association of nirsevimab immunization with hospitalization among infants with RSV LRTD



RESULTS

- Among 49,680 infants born at KPNC, 31,900 healthy term infants met the inclusion criteria. Of these, 15,647 (49.1%) received nirsevimab
- Most of the infants received nirsevimab during November (45.3%) or December (30.8%); mean age (\pm SD) was 2.6 (\pm 2.3) months
- Predominant administration of nirsevimab occurred in outpatient clinical settings (87.5%). Post-immunization, infants were followed for up to 193 days (median: 148 days; IQR: 126–167)
- Among 5,056 infants with at least 1 PCR test during the follow-up period, 1,114 (22.0%) were positive for RSV, with a peak RSV activity in December



RESULTS

Nirsevimab Effectiveness

Primary outcome: First occurrence of PCR-confirmed RSV LRTD

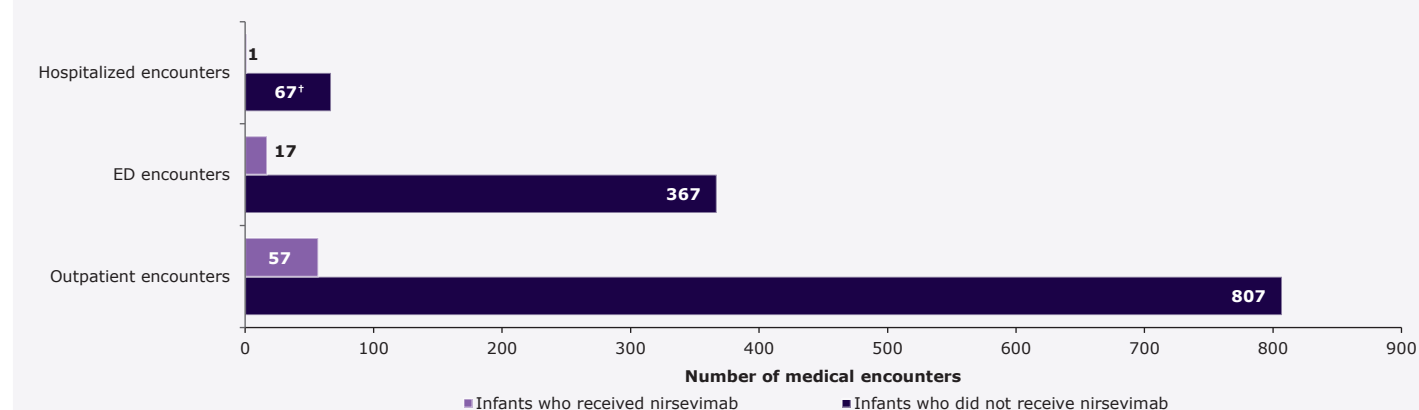
- Number of first episodes of RSV LRTD among infants who received nirsevimab and those who did not receive nirsevimab was **35** (IR [95% CI]: 6.10 [4.38, 8.49]) vs **462** (IR [95% CI]: 58.51 [53.41, 64.09]), respectively
- When compared with infants who did not receive nirsevimab, those who received it showed an adjusted effectiveness of **87.2%** against RSV LRTD (95% CI: 81.7%, 91.1%; **p<0.001**)

Nirsevimab Impact on Healthcare Utilization

Co-primary outcome: Number of medical encounters associated with an RSV LRTD episode

- Among the 35 infants who received nirsevimab and had RSV LRTD, a total of **75** medical encounters were reported; most of these were in outpatient clinics (76% [57/75]) **Figure 1**
 - Mean number of encounters per episode of RSV LRTD: **2.14**
- Of the 462 infants who did not receive nirsevimab and had RSV LRTD, about **1,241** medical encounters were reported; most of these were also in outpatient clinic settings (65% [807/1241]) **Figure 1**
 - Mean number of encounters per episode of RSV LRTD: **2.69**
- Among infants with RSV LRTD, those who received nirsevimab had an adjusted 0.86 fewer mean number of encounters when compared with the infants who did not receive it (**p=0.001**)
 - Linear regression model adjusted for birth month, sex, and race and/or ethnicity

Figure 1: Total medical encounters within RSV LRTD episodes among infants who received nirsevimab vs those who did not receive nirsevimab*



*A total of 75 and 1,241 medical encounters were reported in infants who received nirsevimab vs those who did not receive it, respectively

†There were two non-immunized infants who had 2 hospitalizations each during their RSV LRTD episodes with a total of 67 hospitalizations across all 65 RSV LRTD episodes

Post-hoc Analyses

- Among infants with RSV LRTD, nirsevimab receipt showed an adjusted effectiveness of 98.0% against hospitalization vs non-immunized infants (95% CI: 85.1, 99.7%; **p<0.001**) **Table 1**

Table 1: Sensitivity analysis for infants who received nirsevimab vs those who did not receive nirsevimab

	Received nirsevimab N=15,647		Did not receive nirsevimab N=16,253		Estimated nirsevimab effectiveness % (95% CI) §	p-value*
	n (IP)	IR (95% CI)	n (IP)	IR (95% CI)		
Hospitalized RSV LRTD	1 (<0.001)	0.17 (0.004, 0.97)	65 (0.004)	8.23 (6.35, 10.49)	98.0 (85.1, 99.7)	<0.001

§Estimated as $(1 - HR_{Adj})$ expressed as a percentage; HR_{Adj} (95% CI): 0.020 (0.003, 0.149)

*Test: $H_0: HR_{Adj}=1$



KEY MESSAGES

1

Infants who received nirsevimab had less RSV LRTD with significantly fewer medical encounters and lower hospitalization rates than infants who did not receive nirsevimab

2

These findings support the ACIP's recommendation for eligible infants aged <8 months entering their first RSV season to receive nirsevimab to reduce the risk of RSV infection

†Episode was defined as having at least 1 medical encounter with an LRTD diagnosis in any setting in the 7 days before, and up to 10 days after the positive RSV PCR test

Glossary: ACIP, Advisory Committee on Immunization Practices; CI, confidence interval; ED, emergency department; FDA, Food and Drug Administration; H_0 , null hypothesis; HR_{Adj} , adjusted hazard ratio; ICU, intensive care unit; IP, incidence proportion; IQR, interquartile range; IR, incidence rate per 1,000 person-years; KPNC, Kaiser Permanente Northern California; LRTD, lower respiratory tract disease; PCR, polymerase chain reaction; SD, standard deviation

References: Hsiao A, Hansen J, Fireman B, et al. Effectiveness of Nirsevimab against RSV and RSV-Related Events in Infants. *Pediatrics*. 2025;156(2):e2024069510

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