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Systematic Review

Nirsevimab for Prevention of Respiratory Syncytial Virus Lower Respiratory Tract Infection in Infants: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection (LRTI) and hospitalization in infants. Nirsevimab is a long-acting monoclonal antibody given as a single dose. This systematic review summarizes its efficacy and safety in randomized controlled trials (RCTs).
Methods: RCTs of nirsevimab in infants, reporting medically attended RSV LRTI or hospitalization, were eligible. Data were extracted and synthesized without meta-analysis following the SWiM reporting guideline, with qualitative risk-of-bias appraisal using RoB 2 domains.
Findings: Three RCTs (a phase 2b trial, MELODY, and HARMONIE; 11,001 randomized infants) were included. Efficacy against medically attended RSV LRTI was 70.1% (95% CI 52.3–81.2) in the phase 2b trial, 74.5% (95% CI 49.6–87.1) in MELODY, and 83.2% (95% CI 67.8–92.0) against RSV LRTI hospitalization in HARMONIE. Serious adverse events were similar between groups in the placebo-controlled trials.
Conclusion: Nirsevimab reduced RSV LRTI in infants across three trials, with an acceptable short-term safety profile. Data from Indonesia and tropical settings were not found.

INTRODUCTION

Respiratory syncytial virus (RSV) is a common cause of lower respiratory tract infection (LRTI) in infants and a leading cause of hospitalization in early childhood. Until recently, prevention in infants was restricted to short-acting monoclonal antibody given monthly to high-risk infants.

Nirsevimab is an extended half-life monoclonal antibody that is given as a single intramuscular dose before or during the RSV season. Three randomized controlled trials (RCTs) have reported its efficacy: a phase 2b trial in preterm infants [1], the MELODY trial in late preterm and term infants [2], and the HARMONIE trial, a pragmatic open-label trial in infants in France, Germany, and the United Kingdom [3].

These trials differ in population, comparator, and outcome, ranging from a placebo-controlled trial of medically attended RSV LRTI to a pragmatic trial of RSV-associated hospitalization compared with no intervention.

A structured summary can clarify what is known and what is not.

This systematic review aims to summarize the efficacy and safety of nirsevimab for prevention of RSV LRTI in infants, and to describe how results vary by trial design.

METHODS

1. Design

This systematic review of RCTs was planned using the PICO framework. No protocol was prospectively registered. Results were synthesized without meta-analysis, following the principles of the SWiM reporting guideline [5].

2. Eligibility Criteria

Eligibility criteria are summarized in Table 1. RCTs published in peer-reviewed journals were eligible. Trials were grouped by design: placebo-controlled trials (phase 2b and MELODY) and a pragmatic open-label trial (HARMONIE).

Table 1. Eligibility Criteria (PICO)

Element	Criterion
Population	Infants entering their first RSV season
Intervention	Nirsevimab, single intramuscular dose
Comparator	Placebo or no intervention
Outcomes	Medically attended RSV LRTI; RSV LRTI hospitalization; adverse events
Design	RCT in a peer-reviewed journal

3. Information Sources and Search

Peer-reviewed literature indexed in PubMed was searched in November 2026 through a web search interface, using the terms “nirsevimab,” “respiratory syncytial virus,” “infants,” and “randomized trial”. Publisher abstracts and verified secondary records were used to confirm the content of each trial report.

4. Study Selection

Records were screened against the eligibility criteria by title, abstract, and available full-text information. Selection was performed by a single reviewer.

5. Data Items

Sample size, population, dose, comparator, outcome definitions, efficacy with confidence intervals, antidrug antibodies, and serious adverse events were extracted.

6. Risk-of-Bias Appraisal

Risk of bias was appraised qualitatively using the domains of the RoB 2 tool [6] (randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting), based on information in published abstracts and verified secondary records.

7. Effect Measures

Effect measures were reported as given by each trial, including hazard ratios, risk ratios, vaccine or treatment efficacy, absolute event rates, and mean differences, each with its 95% confidence interval where available. When a trial reported a confidence level other than 95%, this is stated in the text. Measures were not converted between scales, because conversion requires data that were not available in the records reviewed.

8. Missing and Unreported Data

When a result, confidence interval, or safety rate was not available in the records reviewed, it is stated as not available and was not estimated. Where a figure was derived by simple arithmetic from reported values, this is stated in the text and no confidence interval is given.

9. Certainty of the Evidence

A formal certainty-of-evidence rating was not performed. Instead, the consistency of results across trials, the precision of estimates, the directness of the evidence, and the potential for bias were considered narratively when interpreting the findings.

10. Ethical Considerations

This review used only published data from previously reported trials and did not involve new contact with patients. Ethical

approval was therefore not required, and the original trials reported their own ethical approvals and participant consent.

11. Synthesis

Because drugs, populations, durations, comparators, and outcomes differed, a pooled estimate was not calculated. Results are reported as provided by each trial and are tabulated and described narratively.

RESULTS

1. Study Selection

The search identified three RCTs that met the eligibility criteria [1–3]. A correspondence reporting extended follow-up of MELODY was also identified [4] and is described where relevant.

2. Characteristics of Included Trials

The phase 2b trial randomized 1,453 preterm infants (gestational age 29 to <35 weeks) to a single 50 mg intramuscular dose of nirsevimab (n = 969) or placebo (n = 484) [1]. MELODY randomized 1,490 late preterm and term infants to nirsevimab (n = 994) or placebo (n = 496) [2]. HARMONIE randomized 8,058 infants aged up to 12 months, born at or after 29 weeks of gestation, to nirsevimab (n = 4,037) or no intervention (n = 4,021) in France, Germany, and the United Kingdom [3].

Table 2. Characteristics of Included Trials

Trial	Design and population
Phase 2b [1]	1,453 preterm infants; nirsevimab 50 mg IM (n = 969) vs placebo (n = 484)
MELODY [2]	1,490 late preterm and term infants; nirsevimab (n = 994) vs placebo (n = 496)
HARMONIE [3]	8,058 infants aged ≤12 months, ≥29 weeks gestation; nirsevimab (n = 4,037) vs no intervention (n = 4,021); pragmatic, open-label

3. Efficacy against RSV Lower Respiratory Tract Infection

3.1 Phase 2b Trial

In the phase 2b trial, medically attended RSV LRTI occurred in 2.6% (25 infants) with nirsevimab and 9.5% (46 infants) with placebo, an efficacy of 70.1% (95% CI 52.3–81.2). RSV LRTI hospitalization occurred in 0.8% (8) versus 4.1% (20), an efficacy of 78.4% (95% CI 51.9–90.3) [1].

3.2 MELODY

In MELODY, medically attended RSV LRTI occurred in 12 infants (1.2%) with nirsevimab and 25 (5.0%) with placebo, an efficacy of 74.5% (95% CI 49.6–87.1). Hospitalization for RSV LRTI occurred in 6 (0.6%) versus 8 (1.6%), an efficacy of 62.1% (95% CI −8.6 to 86.8; P = 0.07), which was not statistically significant [2]. In an extended report including 3,012 infants, efficacy against medically attended RSV LRTI was 76.4% (95% CI 62.3–85.2) and against hospitalization 76.8% (95% CI 49.4–89.4) [4].

3.3 HARMONIE

In HARMONIE, RSV LRTI hospitalization occurred in 11 infants (0.3%) with nirsevimab and 60 (1.5%) with no intervention, an efficacy of 83.2% (95% CI 67.8–92.0). Very severe RSV LRTI occurred in 5 versus 19 infants (efficacy 75.7%, 95% CI 32.8–92.9). Efficacy by country was 89.6% in France, 74.2% in Germany, and 83.4% in the United Kingdom [3].

Table 3. Efficacy by Trial

Trial	Outcome and efficacy (95% CI)
Phase 2b [1]	Medically attended RSV LRTI: 70.1% (52.3–81.2)
MELODY [2]	Medically attended RSV LRTI: 74.5% (49.6–87.1)
HARMONIE [3]	RSV LRTI hospitalization: 83.2% (67.8–92.0)

4. Safety

In MELODY, serious adverse events occurred in 6.8% (67/987) with nirsevimab and 7.3% (36/491) with placebo, adverse events considered related to treatment occurred in about 1%, and antidrug antibodies were detected in 6.1% versus 1.1% [2]. In HARMONIE, treatment-related adverse events occurred in 86 infants (2.1%) [3]. The records reviewed did not

provide summary safety rates for the phase 2b trial.

Table 4. Selected Safety Findings

Trial	Safety finding
MELODY [2]	SAEs 6.8% vs 7.3%; antidrug antibodies 6.1% vs 1.1%; related AEs about 1%
HARMONIE [3]	Treatment-related AEs in 86 infants (2.1%)

5. Risk-of-Bias Appraisal

The phase 2b trial and MELODY were randomized, double-blind, and placebo-controlled. HARMONIE was pragmatic and open-label, comparing nirsevimab with no intervention; the outcome of hospitalization is objective, but knowledge of allocation may influence testing and care-seeking. HARMONIE was funded by the manufacturers (Sanofi and AstraZeneca). A domain-level RoB 2 judgement requires full-text and protocol review and was not completed.

Table 5. Qualitative Risk-of-Bias Summary

Trial	Appraisal
Phase 2b [1]	Randomized, double-blind, placebo-controlled
MELODY [2]	Randomized, double-blind, placebo-controlled
HARMONIE [3]	Randomized, open-label, pragmatic; industry funded

DISCUSSION

1. Summary of Evidence

Across three RCTs, nirsevimab reduced RSV-related lower respiratory tract infection in infants, with efficacy estimates between 70% and 83% depending on trial and outcome [1–3]. The pragmatic HARMONIE trial supports effectiveness in routine care settings.

2. Differences between Outcomes

The trials used different outcomes: medically attended RSV LRTI in the phase 2b trial and MELODY, and RSV LRTI hospitalization in HARMONIE [1–3]. In MELODY, hospitalization efficacy was imprecise (62.1%, 95% CI −8.6 to 86.8) [2], because there were few events, but the extended report suggested similar efficacy of 76.8% [4].

3. Pragmatic Design

HARMONIE compared nirsevimab with no intervention in routine care and found efficacy against hospitalization consistent with the placebo-controlled trials [3]. The consistency across France, Germany, and the United Kingdom supports generalizability within European settings.

4. Safety

Serious adverse events were similar between groups in MELODY, and treatment-related adverse events were uncommon in MELODY and HARMONIE [2][3]. Antidrug antibodies were more frequent with nirsevimab in MELODY (6.1% vs 1.1%) [2], and their clinical importance was not addressed in the records reviewed.

5. Applicability to Indonesia and Tropical Settings

The trials were conducted in temperate settings with seasonal RSV circulation. The records reviewed did not include data from Indonesia or other tropical countries, where RSV seasonality and risk groups may differ. The applicability of the results there is therefore uncertain.

6. Implications for Practice

The findings support nirsevimab as an effective option for prevention of RSV LRTI in infants. Decisions about use depend on local epidemiology, cost, and availability, and should follow national guidance.

7. Implications for Research

Future research should assess effectiveness in tropical settings, duration of protection, effects on later wheeze, and cost-effectiveness compared with maternal vaccination.

8. Strengths of the Review

This review focused on randomized controlled trials published in major peer-reviewed journals, which are the strongest design for estimating intervention effects. Each trial result was cross-checked against the published abstract or a verified secondary record, and the numbers reported here are those given by the trial authors. The reporting of synthesis without meta-analysis followed a published guideline, and limitations in the methods are described openly.

9. Certainty and Consistency of the Evidence

Considered narratively, the certainty of the evidence depends on three features: the number and size of the trials, the consistency of the direction and size of effects between trials, and the precision of the estimates. Where trials agree in direction and have narrow confidence intervals, the evidence is stronger; where trials disagree or have wide confidence intervals, the evidence is weaker and conclusions should be more cautious. A formal grading of certainty was not undertaken and would be needed before the findings are used to support a guideline recommendation.

10. Generalizability

Trial participants are selected by eligibility criteria and often receive closer monitoring than patients in routine care, so effects seen in trials may differ in practice. The populations in the included trials may differ from patients in Indonesia in baseline risk, access to care, and background treatment, and the findings should be applied with attention to local circumstances.

11. Recommendations for an Updated Review

An updated review suitable for journal submission should register a protocol in a public registry before the search, search several databases such as PubMed, Embase, and the Cochrane Library with an exportable strategy, and screen records independently in duplicate. Data should be extracted from full-text reports and trial registries, risk of bias should be assessed domain by domain with RoB 2, and, where trials are sufficiently similar, a random-effects meta-analysis with an assessment of heterogeneity should be performed. The certainty of evidence for each outcome should then be graded using the GRADE approach.

12. Limitations

Several limitations should be acknowledged. Searching was performed through a web interface rather than an exportable multi-database search and no protocol was registered, so relevant trials may have been missed. Selection and extraction were performed by one reviewer, using published abstracts and verified secondary records. A formal RoB 2 assessment was not completed and no pooled estimate was computed. Only three trials were included, outcome definitions differed between trials, and one trial was open-label with manufacturer funding. The review should be repeated with a documented multi-database search and independent duplicate review before the findings are used for clinical recommendations.

CONCLUSIONS

Nirsevimab reduced RSV-related lower respiratory tract infection in infants in three randomized trials, with efficacy of 70% to 83% and an acceptable short-term safety profile. Data from Indonesia and other tropical settings were not found.

Future work should include a pre-registered, multi-database systematic review with meta-analysis, formal risk-of-bias and certainty-of-evidence assessment, and studies in tropical settings.

Author Contribution Statement

The author performed all aspects of this study.

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