CORRESPONDENCE

# Nirsevimab for Prevention of RSV in Term and Late-Preterm Infants

**TO THE EDITOR:** Nirsevimab, a monoclonal antibody with an extended half-life, is approved by the European Commission and the U.K. Medicines and Healthcare Products Regulatory Agency for the prevention of respiratory syncytial virus (RSV)–associated lower respiratory tract illness in neonates and infants during their first RSV season.[1,2] The phase 3 MELODY trial (ClinicalTrials.gov number, NCT03979313) assessed the efficacy of nirsevimab in infants born at a gestational age of at least 35 weeks. When the coronavirus disease 2019 (Covid-19) pandemic interrupted trial enrollment, efficacy against medically attended RSV-associated lower respiratory tract infection among 1490 participants who had undergone randomization at that point was 74.5% (95% confidence interval [CI], 49.6 to 87.1).[3] However, the analysis was underpowered to determine the efficacy of nirsevimab against hospitalization for RSV-associated lower respiratory tract infection.

Full enrollment in the MELODY trial is now complete. A total of 3012 participants have undergone randomization, in a 2:1 ratio; 1998 infants have received one dose of nirsevimab (at a dose of 50 mg if they weighed <5 kg or at a dose of 100 mg if they weighed ≥5 kg) and 996 have received placebo before their first RSV season (Fig. S1 and Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Inclusion and exclusion criteria are provided in Section S2. The protocol (available at NEJM.org) was approved by the institutional review board at each of the 211 trial sites in a total of 31 countries; all the parents and guardians of the participants provided written informed consent. Full details of the trial conduct are provided in the protocol. The participants were representative of the population of infants at risk for RSV worldwide (Table S2).

The case definition of medically attended RSV-associated lower respiratory tract infection is provided in Table S3. Through 150 days after injection, efficacy against hospitalization for RSV-associated lower respiratory tract infection was 76.8% (95% CI, 49.4 to 89.4) and efficacy against very severe medically attended RSV-associated lower respiratory tract infection was 78.6% (95% CI, 48.8 to 91.0) (Fig. 1). Efficacy against medically attended RSV-associated lower respiratory tract infection (76.4%; 95% CI, 62.3 to 85.2) was consistent with that in the trial primary cohort[3] and when stratified according to hemisphere of residence (northern or southern), age at randomization, sex, race, body weight on day 1, and geographic region (Fig. S2), with no evidence of waning efficacy over 150 days (Fig. S3). Protection was observed against RSV subtypes A and B (Table S4), medically attended lower respiratory tract infection of any cause, and hospitalization for lower respiratory tract infection of any cause (Table S5). Efficacy was consistent with that in a pooled analysis of the phase 2b and phase 3 MELODY trials.[4]

A total of 37 of 1701 nirsevimab recipients and 35 of 849 placebo recipients were hospitalized for lower respiratory tract infection of any cause. With the exclusion of participants who were enrolled in South Africa, where there was no RSV transmission during the Covid-19 pan-

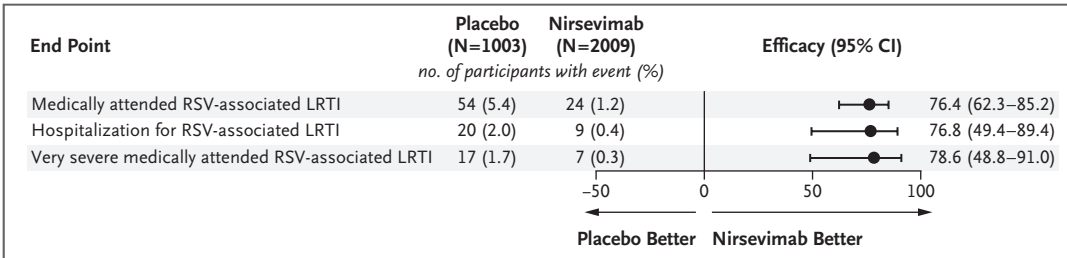


**Figure 1. Incidence of Medically Attended Respiratory Syncytial Virus (RSV)–Associated Lower Respiratory Tract Infection (LRTI) through 150 Days after Injection and Efficacy of Nirsevimab as Compared with Placebo.**

Very severe medically attended RSV-associated LRTI was defined as infection for which hospitalization and supplemental oxygen or intravenous fluids were warranted. Data are from the intention-to-treat population, which consisted of all infants who had undergone randomization.

demic,[5] the number needed to treat to prevent one hospitalization for lower respiratory tract infection of any cause was 53.1 (95% CI, 29.4 to 250.0), a number that was consistent with that in the primary cohort in the MELODY trial.[3] Furthermore, an estimated 57 days of hospitalization for lower respiratory tract infection of any cause were averted for every 1000 infants who received nirsevimab.

Adverse events related to nirsevimab or placebo were reported in 1.3% of the nirsevimab recipients and 1.5% of the placebo recipients through 360 days after injection. Data are shown in Tables S6 and S7.

In term and late-preterm infants, a single dose of nirsevimab provided a consistent level of protection against hospitalization for RSV-associated lower respiratory tract infection and very severe medically attended RSV-associated lower respiratory tract infection during an RSV season.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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1. AstraZeneca AB. Summary of product characteristics: Beyfortus 50 mg/100 mg solution for injection. 2022 (https://www.ema.europa.eu/en/documents/product-information/beyfortus-epar-product-information_en.pdf).
2. Business Wire. MHRA grants approval of Beyfortus (nirsevimab) for prevention of RSV disease in infants. November 9, 2022 (https://www.businesswire.com/news/home/20221109005601/en).
3. Hammitt LL, Dagan R, Yuan Y, et al. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. N Engl J Med 2022;386:837-46.
4. Simões EAF, Madhi SA, Muller WJ, et al. Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomised controlled trials. Lancet Child Adolesc Health 2023;7:180-9.
5. Tempia S, Walaza S, Bhiman JN, et al. Decline of influenza and respiratory syncytial virus detection in facility-based surveillance during the COVID-19 pandemic, South Africa, January to October 2020. Euro Surveill 2021;26:2001600.

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# Safety of Health Care in the Inpatient Setting

**TO THE EDITOR:** In their article on the safety of inpatient health care, Bates and colleagues (Jan. 12 issue)[1] describe events that should not surprise anyone for three key reasons. First, many in the health care field ignored a warning in 1997 that a focus on "human error" according to data regarding patient safety "would delay any real progress on safety for a decade or more."[2] Error-related literature supports rejecting "human error as a cause of accidents and adverse events."[3] However, the patient-safety movement remains fixated on human error instead of complex sociotechnical systems as the cause of preventable harm. Second, research is needed on how clinical care is provided. Billions of dollars have been spent on efforts to understand the human body and to develop treatments, with little investment in understanding how to deliver care.[4] Third, the drivers of the patient-safety movement have excluded investigators who are trained in safety science. This action has forced a reliance on safety practitioners who work in health care with limited formal training in the broader science of safety rather than on investigators who are trained in safety science. Whereas the use of nonexperts to provide clinical care would be viewed as negligence, the use of nonexperts in patient safety is the standard of care.[5]

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1. Bates DW, Levine DM, Salmasian H, et al. The safety of inpatient health care. N Engl J Med 2023;388:142-53.
2. Hollnagel E, Braithwaite J, Wears RL. Resilience, the second story, and progress on patient safety. In: Resilient health care. Boca Raton, FL: CRC Press, 2013;19-26.
3. Read GJM, Shorrock S, Walker GH, Salmon PM. State of science: evolving perspectives on 'human error'. Ergonomics 2021;64:1091-114.
4. Gawande A. The checklist. New Yorker. December 10, 2007 (https://www.newyorker.com/magazine/2007/12/10/the-checklist).
5. Wears R, Sutcliffe K. Still not safe: patient safety and the middle-managing of American medicine. New York: Oxford University Press, 2019.

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**TO THE EDITOR:** Bates et al. provide an update to the Harvard Medical Practice Study from 1991,[1] the seminal research that launched the modern patient-safety movement. The study by Bates et al. follows two other recent studies — one by Eldridge et al.[2] and another by the Office of the Inspector General[3] — that evaluated the current state of patient safety. In these studies, investigators performed manual chart review and reported disappointing progress in the reduction of medical errors.

We think that 32 years is too long to wait for the next report. We posit that the major reason that more progress has not been made regarding safety is the absence of readily available, reliable, and automated measurements of medical errors and adverse medical events. We need the metrics before we can study the effects of interventions. In the era of electronic health records, these measures can be created automatically with the use of audit log data. Examples of this type of measure already exist.[4,5] Automating data collection would allow for updates on patient safety to occur every day in every hospital.

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