

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).

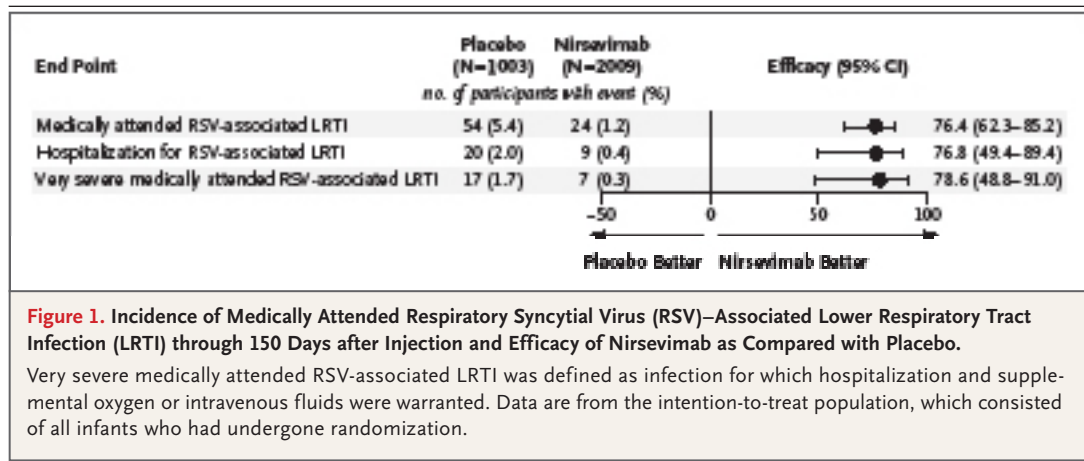
The case definition of medically attended RSV-associated lower respiratory tract infection is provided in Table S3. Through 150 days after injection, efficacy against hospitalization for

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 cohort³ 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 pandemic,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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