REAL-WORLD EVIDENCE

Comparative Analysis Between Beyfortus® and RSVpreF Vaccine for Respiratory Syncytial Virus-Related Hospitalization in Newborns

Funded by the French National Agency for Medicines and Health Products Safety and the French National Health Insurance and published in *JAMA*

RSVpreF, respiratory syncytial virus prefusion F protein.

INDICATION

Beyfortus is indicated for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in:

- Neonates and infants born during or entering their first RSV season.
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

IMPORTANT SAFETY INFORMATION

Contraindication

Beyfortus is contraindicated in infants and children with a history of serious hypersensitivity reactions, including anaphylaxis, to nirsevimab-alip or to any of the excipients.

Please see additional Important Safety Information throughout this summary and accompanying full Prescribing Information.

Beyfortus® (nirsevimab-alip) | 50 mg 100 mg Injection

Beyfortus® (nirsevimab-alip) Pivotal Trial Data[1-6]

In 2 randomized, placebo-controlled pivotal trials, Beyfortus demonstrated efficacy against MA RSV-LRTI and RSV hospitalization[1-4*†]

In Trial 04, Beyfortus exhibited a reduction in MA RSV-LRTI and RSV hospitalization compared to placebo: healthy term and late preterm infants (≥35 wGA)[1-4]

Trial 04 Primary Cohort[‡§‖]

50 mg IM dose if <5 kg weight,
100 mg IM dose if ≥5 kg weight[1]

Primary endpoint: incidence of MA RSV-LRTI through 150 days post 1 dose[1]

↓74.9% RRR

(95% CI: 50.6, 87.3; *P*<0.001)

Beyfortus: 1.2% (12/994)
Placebo: 5.0% (25/496)

Secondary endpoint: incidence of RSV hospitalization through 150 days post 1 dose[1,2]

↓60.2% RRR

(95% CI: -14.6, 86.2; *P*=0.09)

Beyfortus: 0.6% (6/994)
Placebo: 1.6% (8/496)

Trial 04 Full Study Cohort[§]

50 mg IM dose if <5 kg weight,
100 mg IM dose if ≥5 kg weight[1]

Exploratory post hoc analysis of secondary endpoint: incidence of RSV hospitalization through 150 days post 1 dose[2-4]

↓76.8% RRR

(95% CI: 49.4, 89.4)

Beyfortus: 0.4% (9/2,009)
Placebo: 2.0% (20/1,003)

CI, confidence interval; **IM**, intramuscular; **MA RSV-LRTI**, medically attended respiratory syncytial virus lower respiratory tract infection; **RRR**, relative risk reduction; **wGA**, weeks gestational age.

Signs of LRTI involvement included rhonchi, rales, crackles, or wheezing and at least one sign of worsening clinical severity, including at least one of the following: increased respiratory rate, hypoxemia, acute hypoxic or ventilatory failure, new onset apnea, nasal flaring, retractions, grunting, or dehydration due to respiratory distress.[1]

*Results of Trials 04 and 03 for infants entering their first RSV season.[1]
†RSV hospitalization was defined as hospitalization for LRTI with a positive RSV test.[1]
‡Primary Cohort: 1,490 healthy term and late preterm infants (≥35 wGA) in Trial 04.[1]
§During Trial 04, the COVID-19 pandemic interrupted trial enrollment. The efficacy analysis is based on the Primary Cohort, which included those participants enrolled prior to the pause due to COVID-19. Trial 04 continued monitoring the Primary Cohort and included an additional 1,522 subjects enrolled after the pause to comprise the full study cohort. The full study cohort included 3,012 infants randomized to receive Beyfortus or placebo in the post hoc analysis.[4]
‖Efficacy for MA RSV-LRTI based on RRR against placebo adjusted for age at randomization.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

- **Hypersensitivity Reactions Including Anaphylaxis:** Serious hypersensitivity reactions have been reported following Beyfortus administration. These reactions included urticaria, dyspnea, cyanosis, and/or hypotonia. Anaphylaxis has been observed with human immunoglobulin G1 (IgG1) monoclonal antibodies. If signs and symptoms of anaphylaxis or other clinically significant hypersensitivity reactions occur, initiate appropriate treatment.

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In Trial 03, Beyfortus® exhibited a reduction in MA RSV-LRTI and RSV hospitalization compared to placebo: healthy preterm infants (≥29 to <35 wGA)[1,5]

Trial 03*†

50 mg IM dose regardless of weight[1]

Primary endpoint: incidence of MA RSV-LRTI through 150 days post 1 dose[1]

↓70.1% RRR

(95% CI: 52.3, 81.2; *P*<0.001)

Beyfortus: 2.6% (25/969)
Placebo: 9.5% (46/484)

Secondary endpoint: incidence of RSV hospitalization through 150 days post 1 dose[1,5]

↓78.4% RRR

(95% CI: 51.9, 90.3; *P*<0.001)

Beyfortus: 0.8% (8/969)
Placebo: 4.1% (20/484)

Trial 03 Post Hoc Analysis‡

Subgroup of infants <5 kg receiving 50 mg IM dose[1]

Exploratory post hoc analysis of secondary endpoint: incidence of MA RSV-LRTI through 150 days post 1 dose[1,6]

↓86.2% RRR

(95% CI: 68.0, 94.0)

Beyfortus: 1.2% (7/570)
Placebo: 9.0% (26/290)

This subgroup included 860 infants weighing <5 kg who were randomized to receive 50 mg IM dose of Beyfortus (coinciding with the approved weight-based dose) or placebo.

The most common adverse reactions reported at an incidence higher than placebo in the Safety Population (Trial 04 and Trial 03) were rash (0.9%) and injection site reactions (0.3%)[1§]

Trial 04 and Trial 03 were pooled to evaluate the safety of Beyfortus (N=2,570) compared to placebo (N=1,284).[1]

- Adverse reactions were reported in 1.2% of infants who received Beyfortus; most (97%) of adverse reactions were mild to moderate in severity

*1,453 preterm infants (≥29 to <35 wGA) in Trial 03.[1]
†Efficacy for MA RSV-LRTI based on RRR against placebo adjusted for age at randomization and hemisphere.[1]
‡860 infants from the full study cohort of 1,453 healthy preterm infants in Trial 03 were analyzed in a post hoc analysis. For infants in their first RSV season, the recommended dose is 50 mg for infants <5 kg or 100 mg for infants ≥5 kg via IM injection.[1,6]
§The Safety Population includes all infants who received the recommended dose of Beyfortus in Trials 04 and 03: Primary and Safety cohorts from Trial 04; infants who weighed <5 kg and who received the recommended dose of Beyfortus (single 50 mg IM dose) in Trial 03.[1]

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Real-world evidence: Comparative analysis between Beyfortus® and the RSVpreF vaccine[7]

Prevention of RSV hospitalization during the 2024-2025 season[7]*

	EPI-PHARE study design[7]
Study population	Infants born between September 1 and December 31, 2024, in mainland France, who were immunized either via Beyfortus or maternal vaccination (RSVpreF) and were discharged from the hospital on or after October 1, 2024. Follow-up ended at the time of RSV hospitalization, unrelated death, or on February 28, 2025.
RSV season	For the 2024-2025 RSV season, daily RSV hospitalizations occurred from October 2024 to February 2025 and peaked from mid-November 2024 to early January 2025.
Number of subjects	In matched analysis: N=42,560; n=21,280 in each group.
Immunization campaign	• In France, Beyfortus was recommended during the first RSV season for all infants born on or after January 1, 2024† • Maternal vaccination with RSVpreF was recommended at 32 to 36 weeks' gestation from September 1, 2024, to January 31, 2025‡
Methodology	Infants were matched 1:1 based on discharge day, sex, gestational age, and region of residence. Weighted conditional Cox proportional hazards models were fitted to account for the matched design and estimate hazard ratios (HRs) with 95% CIs.§‖
Key assessment	Hospitalization for RSV-associated LRTI.

EPI-PHARE, French National Agency for Medicines and Health Products Safety and French National Health Insurance; **ICD-10**, International Classification of Diseases, Tenth Revision.

*RSV hospitalization was defined as hospitalization for RSV-associated LRTI identified using ICD-10 RSV codes for acute bronchiolitis (J210), pneumonia (J121), and acute bronchitis (J205).[7]

†The immunization campaign began on September 15, 2024.[7]

‡The national campaign concluded on January 31, 2025.[7]

§For each day between October 1 and December 31, 2024, every infant born to a mother vaccinated with the RSVpreF vaccine was matched to an infant who received Beyfortus on the same maternity discharge day, using random sampling without replacement. This process achieved a match rate of 92%.[7]

‖Infants were excluded if they were discharged from the maternity ward before October 1, 2024.[7]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

- **Use in Individuals with Clinically Significant Bleeding Disorders:** As with other IM injections, Beyfortus should be given with caution to infants and children with thrombocytopenia, any coagulation disorder or to individuals on anticoagulation therapy.

Most common adverse reactions with Beyfortus were rash (0.9%) and injection site reactions (0.3%).

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Study results[7]

Primary outcome: RSV hospitalization

By matched cohort:

Beyfortus®: 1.0% (212/21,280)

RSVpreF vaccine: 1.3% (269/21,280)

26% lower observed risk of RSV hospitalization with Beyfortus compared to maternal vaccination with RSVpreF

(aHR: 0.74; 95% CI: 0.61, 0.88)

Median follow-up was 84 days (IQR: 70–99 days)

The difference in hospitalization risk varied over time. Beyfortus showed:

- Higher risk from Day 0 to Day 7 (aHR: 2.94; 95% CI: 1.19, 7.69)
- No significant difference from Day 8 to Day 30 (aHR: 0.79; 95% CI: 0.60, 1.05)
- Lower risk from Day 31 to Day 60 (aHR: 0.62; 95% CI: 0.45, 0.84)
- Lower risk after Day 60 (up to Day 148) (aHR: 0.51; 95% CI: 0.30, 0.86)

The adjusted hazard ratio (aHR) was derived using an inverse probability of treatment weighting method that was applied to the matched dataset to further balance the residual covariates.[7]

The findings in this report are subject to limitations[7]:

- As the RSVpreF vaccine became available in September and matching was based on birth date, infants were by design born later in the RSV season, which may limit generalizability to those born earlier
- Conducted during the first season of maternal RSVpreF vaccination in France, when eligibility was limited to 32 to 36 weeks' gestation, unlike the WHO's recommendation for vaccination beginning at 28 weeks' gestation. Findings reflect early national experience in France and require reevaluation in future studies and settings
- Follow-up was limited to one RSV season, so durability of protection could not be assessed
- Administrative data did not allow analysis by RSV subtypes
- The subgroup analyses were not stratified beyond 60 days of follow-up, limiting insights into longer-term differences between the 2 preventive strategies
- Potential unmeasured confounding factors (eg, parental health-seeking behavior, household smoking, or daycare attendance) could not be excluded

This study did not assess the safety of Beyfortus or RSVpreF.[7]

IQR, interquartile range; **WHO**, World Health Organization.

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Scan to learn more about Beyfortus

Speak to your Sanofi representative for more information

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Most common adverse reactions with Beyfortus were rash (0.9%) and injection site reactions (0.3%).

Please see accompanying full Prescribing Information.

References: 1. Beyfortus (nirsevimab-alip). Prescribing Information. Sanofi. **2.** US Food and Drug Administration. Biologics license application 761328. June 8, 2023. Accessed March 10, 2026. https://www.fda.gov/media/169226/download **3.** Muller WJ, Madhi SA, Nuñez BS, et al; MELODY Study Group. Nirsevimab for prevention of RSV in term and late-preterm infants. *N Engl J Med.* 2023;388(16):1533-1534. **4.** Muller WJ, Madhi SA, Nuñez BS, et al; MELODY Study Group. Nirsevimab for prevention of RSV in term and late-preterm infants. *N Engl J Med.* 2023;388(16)(suppl):1533-1534. **5.** Griffin MP, Yuan Y, Takas T, et al. Single-dose nirsevimab for prevention of RSV in preterm infants. *N Engl J Med.* 2020;383(5):415-425. **6.** US Food and Drug Administration. Advisory Committee Briefing Document: nirsevimab. May 17, 2023. Accessed March 10, 2026. https://www.fda.gov/files/advisory%20committees/published/20230608-AMDAC-Backgrounder-AZ.pdf **7.** Jabagi MJ, Bertrand M, Gabet A, et al. Nirsevimab vs RSVpreF vaccine for respiratory syncytial virus-related hospitalization in newborns. *JAMA*. 2025 Dec 22:e2524082.

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MAT-US-2601350-v1.0-03/2026