# VRS: monoclonales “al ataque”

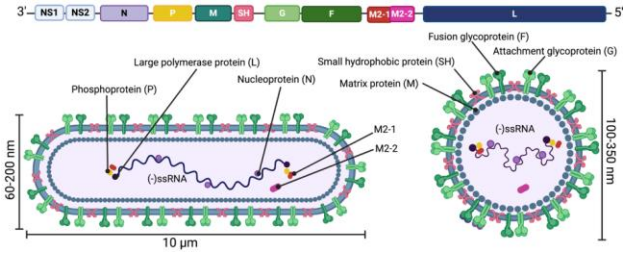
**Antonio Iofrío De Arce**

Pediatra CS El Ranero (Murcia)

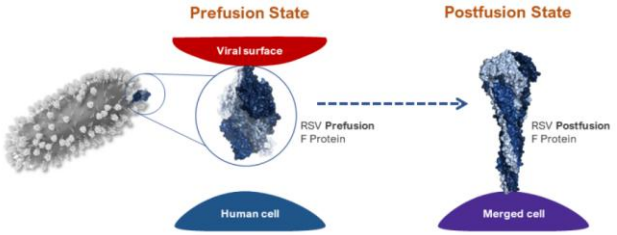
Secretario del CAV-AEP


Antonio Iofrío De Arce

- He participado en actividades formativas organizadas por AZ, GSK, MSD, Sanofi y Pfizer
- He participado en consultoría de asesoramiento para GSK y Pfizer
- He recibido apoyo de GSK, Pfizer y Sanofi para asistir a actividades formativas




Sanz Muñoz , et al. Rev Esp Quimioter 2024;37(3):209-220




Fuente: NIAID


**1956-7** | **1982-86** | **1998-9** | **2013** | **2022-23** | **2025**


Fuente: CDC

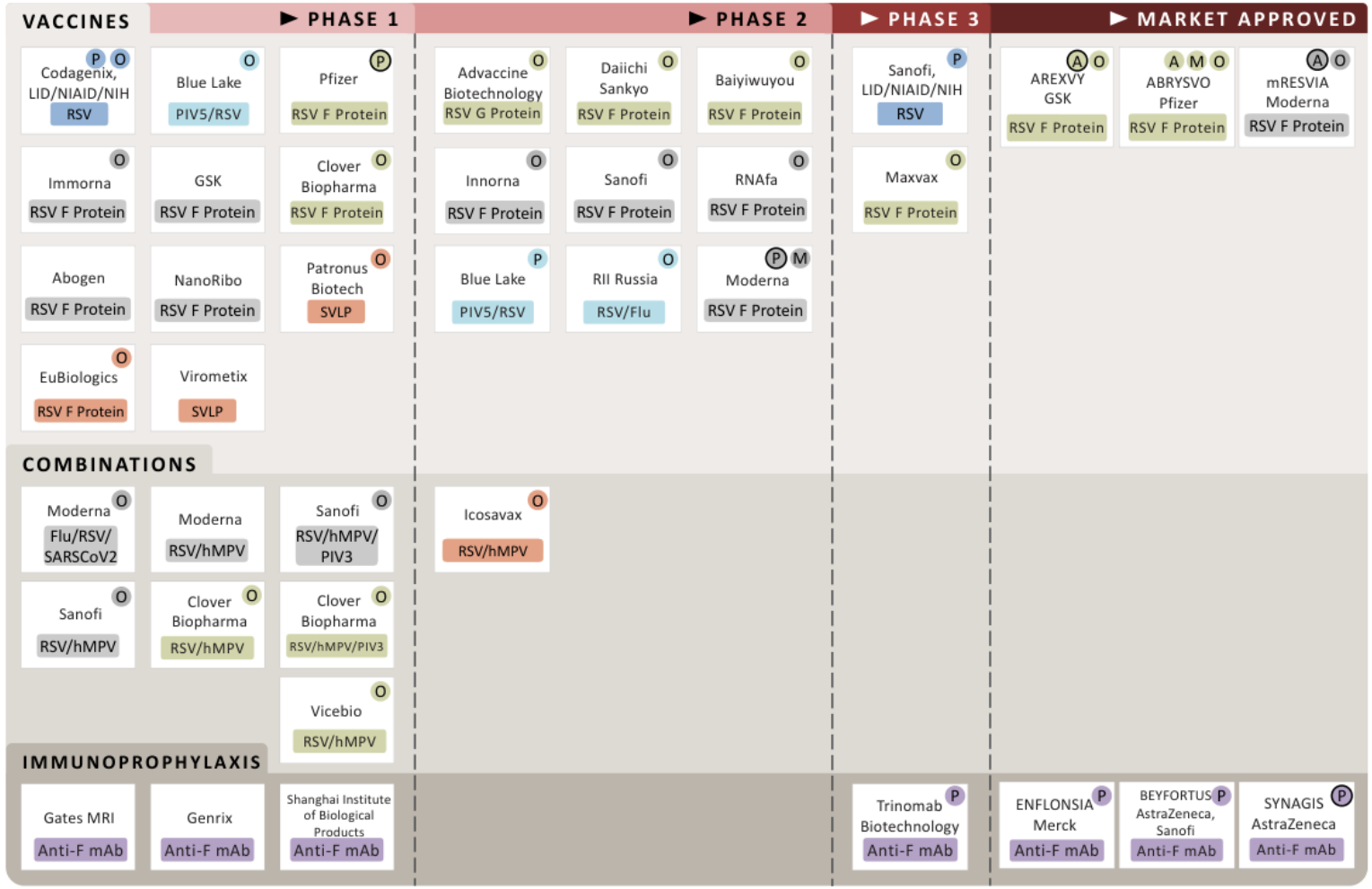


Elaboración propia

# RSV Vaccine and mAb Snapshot

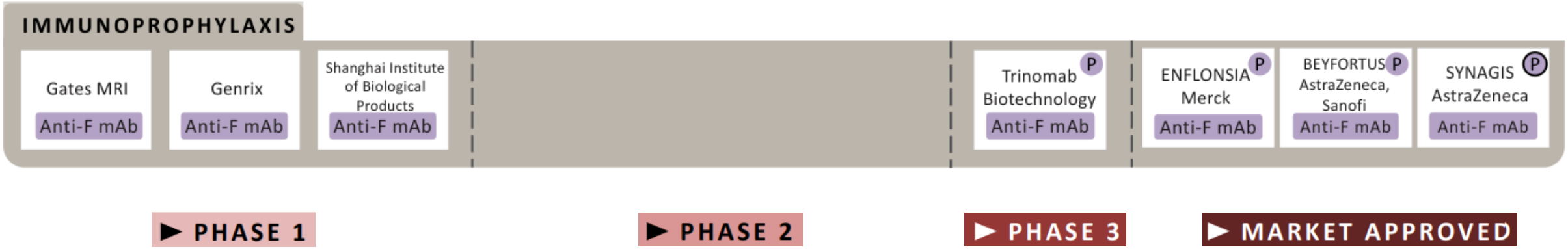
P =PEDIATRIC M =MATERNAL
A =ADULT O =OLDER ADULT
◯ =LIMITED TO INCREASED RISK

PLATFORM KEY:
=LIVE/CHIMERIC =mAb
=VECTORED =PARTICLE
=SUBUNIT =NUCLEIC ACID

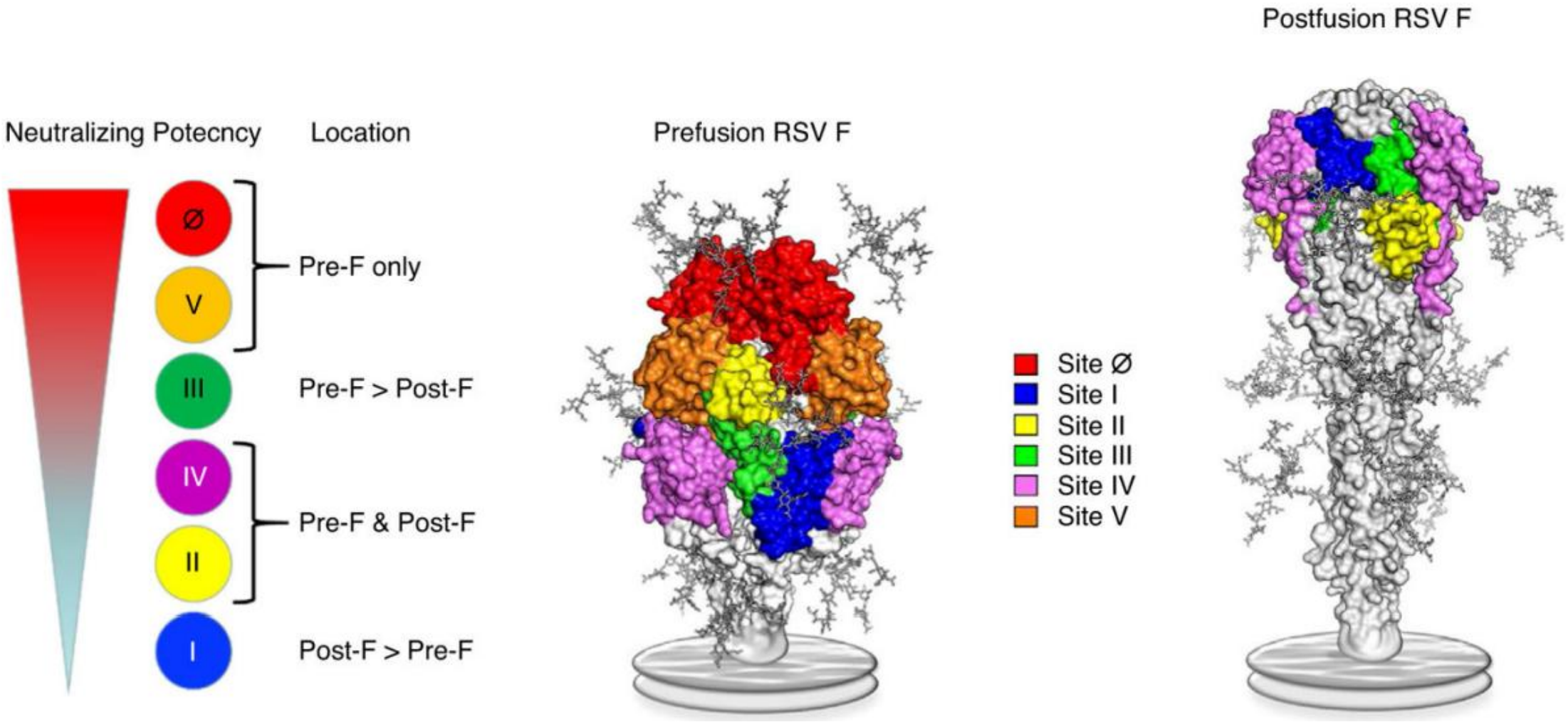



*SVLP = Synthetic virus-like particle **UPDATED: December 10, 2025** https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH




Modificado de https://media.path.org/documents/RSV-snapshot_10DEC2025_clinical-stage.pdf

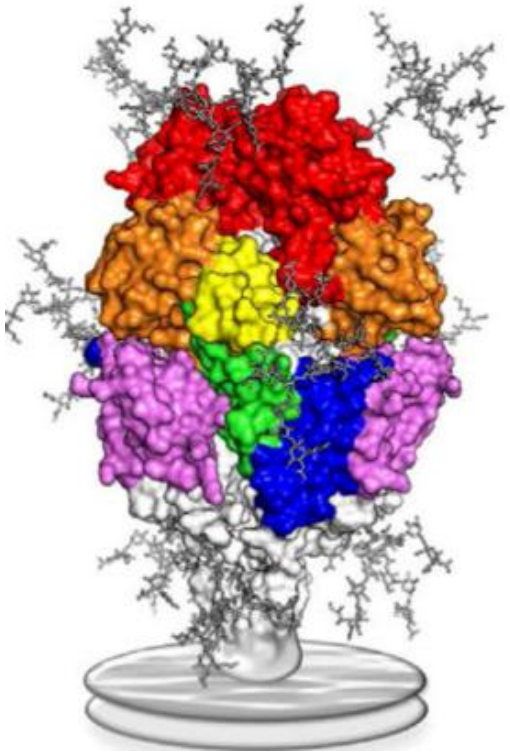



Graham BS. Curr Opin Virol. 2017;23:107-12.

**Nirsevimab, TNM001**

Site Ø
Site I
Site II
Site III
Site IV
Site V

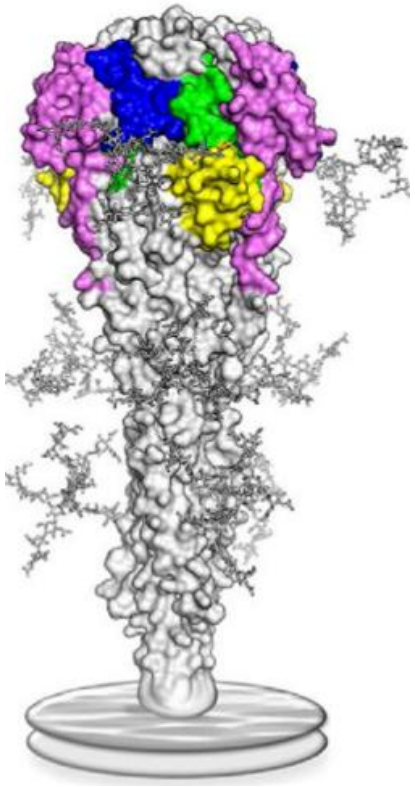
Prefusion RSV F



**Palivizumab**

**Clesrovimab**

Postfusion RSV F



Modificado de Graham BS. Curr Opin Virol. 2017;23:107-12.

| FECHA DE APROBACIÓN (FDA, Comisión Europea) | | | |
|---|---|---|---|
| | **PALIVIZUMAB (SYNAGIS®)** | **NIRSEVIMAB (BEYFORTUS®)** | **CLESROVIMAB (ENFLONSIA®)** |
| |  |  |  |
| | 19 junio 1998 | 17 julio 2023 | 9 junio 2025 |
| | 13 agosto 1999 | 31 octubre 2022 | - |

Elaboración propia

| PRESENTACIÓN Y POSOLOGÍA (fichas técnicas) | | |
|---|---|---|
| **PALIVIZUMAB (SYNAGIS®)**   | **NIRSEVIMAB (BEYFORTUS®)**   | **CLESROVIMAB (ENFLONSIA®)**   |
| Vial 50 mg/0,5 ml<br>Vial 100 mg/1 ml | Vial 50 mg/0,5 ml<br>Vial 100 mg/1 ml | Vial 105 mg/0,7 ml |
| 15 mg/kg (0,15 ml/kg) **mensual**, antes del inicio y durante la temporada del VRS | **Dosis única por temporada**<br><br>1.ª temporada VRS:<br><5 kg: 50 mg<br>≥5 kg: 100 mg<br><br>2.ª temporada (<24 m riesgo):<br>200 mg (2x100 mg) | **Dosis única por temporada**<br><br>1.ª temporada VRS:<br>1 dosis 105 mg<br>(independiente del peso) |

Elaboración propia

| INDICACIONES (fichas técnicas) | | |
|---|---|---|
| **PALIVIZUMAB (SYNAGIS®)**   | **NIRSEVIMAB (BEYFORTUS®)**   | **CLESROVIMAB (ENFLONSIA®)**   |
| Niños con alto riesgo de enfermedad por VRS:<br>• RNPT ≤35 sg y <6 meses de edad al inicio de la estación de riesgo de infección por VRS<br>• <2 años de edad que hayan requerido tratamiento para la DBP en los últimos 6 meses<br>• <2 años de edad con cardiopatía congénita hemodinámicamente significativa | Prevención de IRTI-VRS en:<br>• Neonatos y lactantes durante su primera temporada del VRS<br>• Niños de hasta 24 meses de edad que siguen siendo vulnerables a la enfermedad grave por VRS durante su segunda temporada de VRS | Prevención de IRTI-VRS en:<br>• Neonatos y lactantes durante su primera temporada del VRS |

Elaboración propia

| EFECTOS ADVERSOS (fichas técnicas) | | |
|---|---|---|
| **PALIVIZUMAB (SYNAGIS®)**   | **NIRSEVIMAB (BEYFORTUS®)**   | **CLESROVIMAB (ENFLONSIA®)**   (Ctrl) |
| Muy frecuentes (≥1/10): exantema, fiebre<br><br>Frecuentes (1-10/100): dolor, enrojecimiento o hinchazón en el punto de inyección, apneas u otras dificultades respiratorias | Exantema leve a moderado (0,7%) en los 14 días posteriores<br><br>Fiebre (0,5%) y reacciones en el lugar de la inyección (0,3%) en los 7 días posteriores | Eritema (3,7%) e hinchazón (2,7%) en el lugar de la inyección, erupción cutánea (2,3%) |

Elaboración propia

| Participantes en los ensayos | NIRSEVIMAB | CLESROVIMAB |
|---|---|---|
| **Sanos (vs. placebo)** | Fase 3 (**MELODY**): RNPT ≥35 SEG y término durante su primer año<br><br>Fase 2b: RNPT ≥29-<35 SEG en su primera temporada de VRS | Fase 2b/3 MK-1654-004 (**CLEVER**): RNPT ≥29 SEG y término durante su primer año |
| **Riesgo (vs. palivizumab)** | Fase 2/3 (**MEDLEY**): RNPT <35 SEG durante su primera temporada de VRS, o con EPC o CHS durante su segunda temporada de VRS | Fase 3 MK-1654-007 (**SMART**): RNPT ≤35 SEG, o con EPC o CHS durante su primer año |

SEG: semanas de edad gestacional. EPC: enfermedad pulmonar crónica. CHS: cardiopatía hemodinámicamente significativa

Elaboración propia

| Ensayos pivotales | NIRSEVIMAB (MELODY) | CLESROVIMAB (CLEVER) |
|---|---|---|
| **Objetivos primarios** | Incidencia de IRTI-VRS atendidas médicamente hasta 150 días después de la dosis, definida como:<br>1) ≥1 de roncus, estertores, crepitantes, sibilancias<br>2) Criterios gravedad: ≥1 de tiraje, hipoxemia, taquipnea, apnea, taquipnea o deshidratación debido a síntomas respiratorios, y<br>3) Confirmada por RT-PCR | Incidencia de IRTI-VRS atendidas médicamente hasta 150 días después de la dosis, definida como:<br>1) tos o dificultad para respirar, y<br>2) ≥1 de sibilantes, estertores, crepitantes, o de criterios de gravedad: tiraje, hipoxemia, taquipnea o deshidratación debido a síntomas respiratorios, y<br>3) Confirmada por RT-PCR |
| **Objetivos secundarios** | Incidencia de hospitalizaciones por VRS confirmado por RT-PCR hasta 150 días , seguridad hasta 365 días | |

Elaboración propia

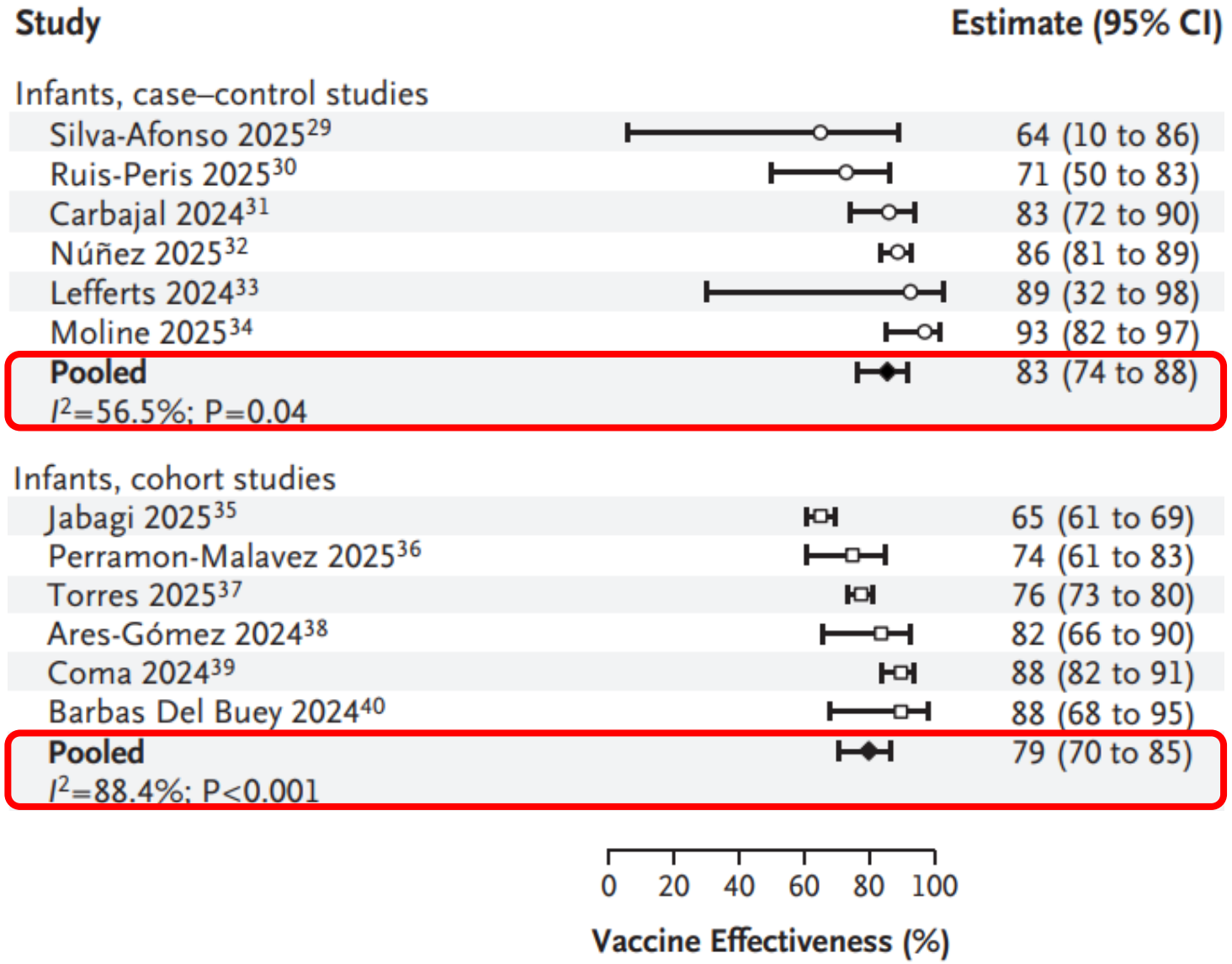

Beyfortus®
50 mg
solution for injection in pre-filled syringe
nirsevimab
Intramuscular use
1 pre-filled syringe
sanofi

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

# Updated Evidence for Covid-19, RSV, and Influenza Vaccines for 2025–2026

J. Scott,[1] M.S. Abers,[2] H.K. Marwah,[3] N.C. McCann,[4] E.A. Meyerowitz,[2] A. Richterman,[5] D.F. Fleming,[6] E.J. Holmes,[6] L.E. Moat,[6] S.G. Redepenning,[6] E.A. Smith,[6] C.J. Stoddart,[6] M.E. Sundaram,[7] A.K. Ulrich,[6] C. Alba,[8] C.J. Anderson,[6] M.K. Arpey,[6] E. Borre,[9] J. Ladines-Lim,[5] A.J. Mehr,[6] K. Rich,[9] C. Watts,[5] N.E. Basta,[10] J. Jarolimova,[11] R.P. Walensky,[12] and C.M. Dugdale[13]



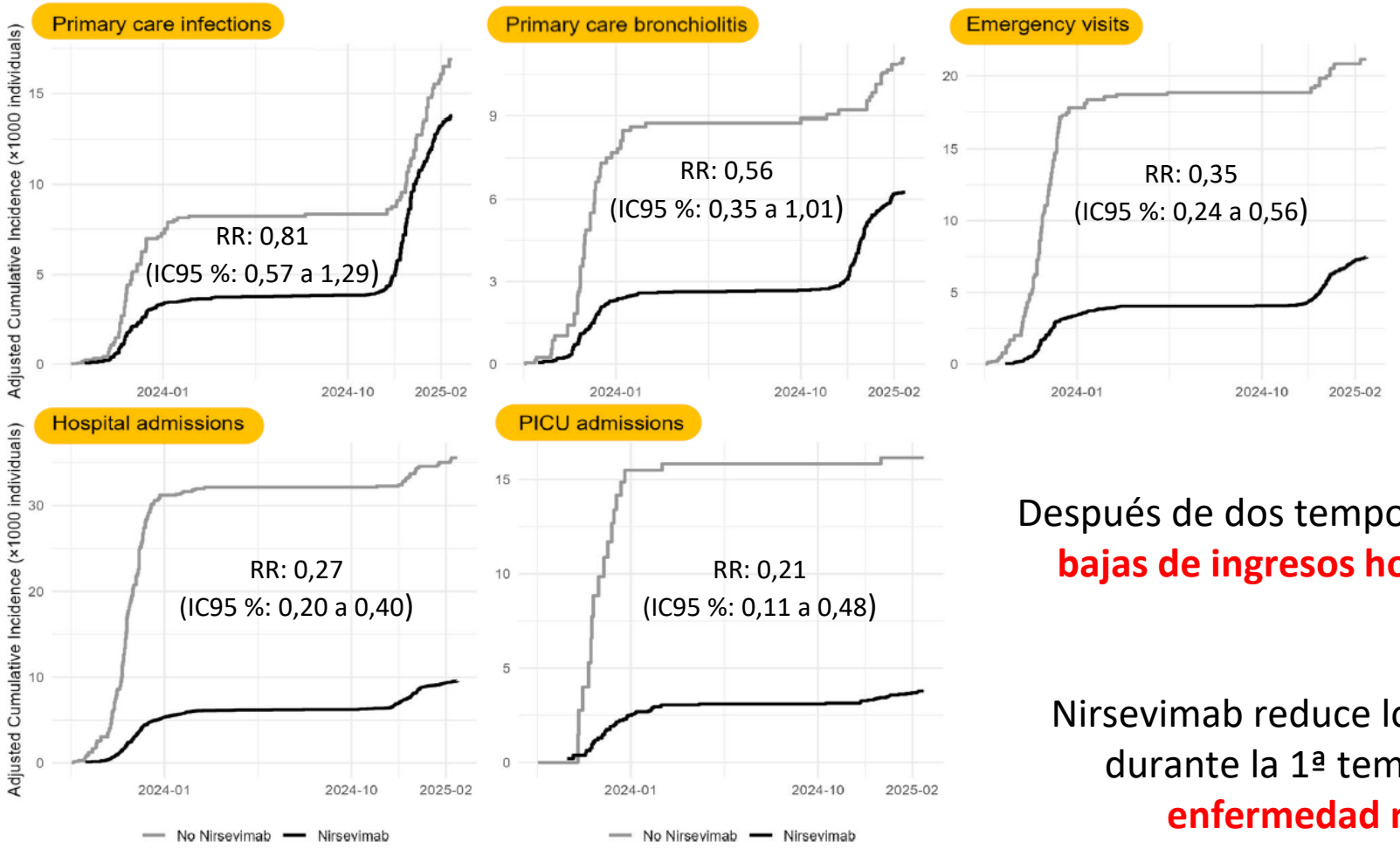

Scott J, *et al*. Updated Evidence for Covid-19, RSV, and Influenza Vaccines for 2025-2026. N Engl J Med. 2025;393(22):2221-2242.

European Journal of Pediatrics (2025) 184:616
https://doi.org/10.1007/s00431-025-06440-x

RESEARCH

# Impact of nirsevimab immunoprophylaxis on respiratory syncytial virus-related outcomes in hospital and primary care after two consecutive seasons: a population-based retrospective cohort study in infants in their second year of life in Catalonia, Spain

Ermengol Coma[1,2] · Montserrat Martínez-Marcos[3] · Eduardo Hermosilla[1,2] · Jacobo Mendioroz[4] · Anna Reñé[1] · Francesc Fina[1,2] · Aida Perramon-Malavez[5] · Clara Prats[5] · Andrés Antón[6] · Antoni Soriano-Arandes[7] · Carmen Cabezas[8]




Después de dos temporadas, todavía encontramos **tasas más bajas de ingresos hospitalarios y en UCIP en el grupo de nirsevimab**

Nirsevimab reduce los resultados graves asociados al VRS durante la 1ª temporada **sin aumentar el riesgo de enfermedad más grave en la 2ª temporada**

Coma E, et al. Eur J Pediatr. 2025;184(10):616.

# Second-season Impact of Nirsevimab

## *Clinical Outcomes of RSV Disease in Patients Immunized During Their First Season*

*Isabel González-Bertolín, MD, PhD,* Sonia Alcolea, BSc,*†‡ Patricia Alonso, MD, PhD,§ María Arroyas, MD, PhD,§¶ Isabel Fernández Castiella, MD,* Iciar Echavarren, MD,* Maria Iglesias-Caballero, PhD,‖ Inmaculada Casas, PhD,‡‖ María Luz García-García, MD, PhD,†‡¶ and Cristina Calvo, MD, PhD‡**††‡‡*

*The Pediatric Infectious Disease Journal* • Volume 44, Number 10, October 2025

**TABLE 1.** Patients' Demographic, Clinical and Laboratory Data

| | Non-nirsevimab (n = 196) | Nirsevimab (n = 34) | *P* Values |
|---|---|---|---|
| | Absolute Frequencies (%) | | |
| Sex (male) | 121 (62) | 18 (53) | 0.34 |
| Prematurity or chronic diseases | 21 (12) | 1 (3) | 0.14 |
| Prior respiratory admission | 36 (21) | 4 (12) | 0.34 |
| Fever | 152 (78) | 28 (85) | 0.49 |
| Viral coinfection | 52 (26) | 6 (28) | 0.62 |
| Oxygen supplementation | 179 (92) | 33 (97) | 0.48 |
| High-flow oxygen | 84 (43) | 10 (29) | 0.18 |
| Noninvasive ventilation | 17 (9) | 0 (0) | 0.08 |
| ICU admission | 18 (9) | 1 (3) | 0.32 |
| Antibiotic therapy | 91 (47) | 1 (33) | 0.18 |
| | Mean (SD) | | |
| Leukocytes (/mm$^3$) | 12291 (5607) | 8679 (8019) | 0.06 |
| CRP value (mg/L) | 36.0 (53.2) | 38.2 (35.7) | 0.74 |
| Age (months) | 12.6 (5) | 13.3 (3.3) | 0.45 |
| | Median (IQR) | | |
| Fever duration (days) | 3 (3) | 3 (4) | 0.35 |
| Temperature (°C) | 39.0 (0.8) | 38.8 (0.7) | 0.55 |
| Length of hospitalization (days) | 4 (3) | 4 (3) | 0.58 |
| Oxygen support duration (days) | 4 (3.5) | 3 (3) | 0.16 |
| ICU stay length (days) | 3 (2.25) | 2 (0) | 0.51 |

Non-nirsevimab: children not immunized with nirsevimab during their first RSV season. Nirsevimab: children who received nirsevimab more than 6 months prior. Data are presented as the median with the IQR in the parentheses, as the mean with the SD in the parentheses, or as absolute frequencies with the percentage in parentheses.

CRP indicates C-reactive protein; ICU, intensive care unit.

González-Bertolín I, *et al*. Pediatr Infect Dis J. 202544(10):1009-1011.

THE LANCET
Infectious Diseases

# Impact of universal nirsevimab prophylaxis in infants on hospital and primary care outcomes across two respiratory syncytial virus seasons in Galicia, Spain (NIRSE-GAL): a population-based prospective observational study

*Josefina L Razzini*, Iago Giné-Vázquez*, Jing Jin*, María-Isolina Santiago-Pérez, Olaia Pérez-Martínez, María-Teresa Otero-Barrós, Nuria Suárez-Gaiche, Rolf Kramer, Leticia Platero-Alonso, Rosa-María Álvarez-Gil, Olga-María Ces-Ozores, Victoria Nartallo-Penas, Susana Mirás-Carballal, Marta Piñeiro-Sotelo, Juan-Manuel González-Pérez, Carmen Rodríguez-Tenreiro-Sánchez, Ángela Manzanares-Casteleiro, Ana Dacosta-Urbieta, Cintia Álvarez-Smith, Irene Rivero-Calle, Antonio Salas, Carmen Durán-Parrondo, Narmeen Mallah*, Federico Martinón-Torres**

Lactantes nacidos entre Oct 2023-Mar 2024 elegibles a nirsevimab (n=12 492) (cobertura: 94,4 %)
Seguimiento durante su primera y segunda temporada de VRS

Razzini JL, *et al*. Lancet Infect Dis. 2026:S1473-3099(25)00742-X

| | First RSV season (Oct 2, 2023–April 14, 2024) | | | | | Second RSV season (Sept 30, 2024–April 13, 2025) | | | | | Up to 18 months follow-up (Oct 2, 2023–April 13, 2025) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Obs | Exp | Av | NNI | Relative change | Obs | Exp | Av | NNI | Relative change | Obs | Exp | Av | NNI | Relative change |
| **First hospitalisation** | | | | | | | | | | | | | | | |
| RSV-related LRTI | 57 | 407 | 350 | 36 | −85·9% (−90·0 to −80·2) | 85 | 187 | 102 | 123 | −55·3% (−74·3 to −22·5) | 142 | 716 | 574 | 22 | −80·4% (−86·4 to −71·6) |
| LRTI | 220 | 547 | 327 | 39 | −59·8% (−69·8 to −46·5) | 141 | 151 | 10 | 1250 | −9·3% (−43·9 to 46·4) | 399 | 767 | 368 | 34 | −48·1% (−59·7 to −33·1) |
| Acute bronchitis or bronchiolitis | 177 | 432 | 255 | 49 | −59·0% (−72·9 to −37·9) | 54 | 91 | 37 | 338 | −40·8% (−68·7 to 12·0) | 250 | 601 | 351 | 36 | −58·7% (−71·3 to −40·6) |
| Pneumonia | 22 | 46 | 24 | 521 | −53·1% (−71·1 to −23·9) | 55 | 49 | −6 | −2082 | 9·1% (−35·8 to 85·3) | 87 | 95 | 8 | 1562 | −11·0% (−38·2 to 28·1) |
| All-cause | 1539 | 1932 | 393 | 32 | −20·3% (−34·4 to −3·1) | 280 | 274 | −6 | −2082 | 1·6% (−19·5 to 28·3) | 2042 | 2237 | 195 | 65 | −8·7% (−23·9 to 9·5) |
| **First recurrent hospitalisation** | | | | | | | | | | | | | | | |
| RSV-related LRTI | 2 | 9 | 7 | 1785 | −79·7% (−96·3 to 12·5) | 3 | 11 | 8 | 1562 | −78·2% (−93·6 to −25·6) | 5 | 28 | 23 | 544 | −85·5% (−94·4 to −61·9) |
| LRTI | 12 | 47 | 35 | 357 | −74·7% (−88·2 to −45·9) | 14 | 35 | 21 | 595 | −62·4% (−79·6 to −30·9) | 26 | 101 | 75 | 167 | −75·5% (−85·2 to −59·4) |
| Acute bronchitis or bronchiolitis | 6 | 20 | 14 | 893 | −75·9% (−93·0 to −17·5) | 4 | 10 | 6 | 2082 | −76·9% (−94·4 to −5·3) | 10 | 39 | 29 | 431 | −81·6% (−92·4 to −55·2) |
| Pneumonia | 1 | .. | .. | .. | NC | 2 | .. | .. | .. | NC | 3 | .. | .. | .. | NC |
| All-cause | 257 | 363 | 106 | 118 | −29·0% (−41·7 to −13·6) | 155 | 168 | 13 | 961 | −7·4% (−27·9 to 19·0) | 538 | 642 | 104 | 121 | 16·0% (−27·8 to −2·3) |

Razzini JL, *et al*. Lancet Infect Dis. 2026:S1473-3099(25)00742-X

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Obs | Exp | Av | NNI | Relative change | Obs | Exp | Av | NNI | Relative change | Obs | Exp | Av | NNI | Relative change |
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| RSV-related LRTI | 57 | 407 | 350 | 36 | −85·9% (−90·0 to −80·2) | 85 | 187 | 102 | 123 | −55·3% (−74·3 to −22·5) | 142 | 716 | 574 | 22 | −80·4% (−86·4 to −71·6) |
| LRTI | 220 | 547 | 327 | 39 | −59·8% (−69·8 to −46·5) | 141 | 151 | 10 | 1250 | −9·3% (−43·9 to 46·4) | 399 | 767 | 368 | 34 | −48·1% (−59·7 to −33·1) |
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| Pneumonia | 22 | 46 | 24 | 521 | −53·1% (−71·1 to −23·9) | 55 | 49 | −6 | −2082 | 9·1% (−35·8 to 85·3) | 87 | 95 | 8 | 1562 | −11·0% (−38·2 to 28·1) |
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| **First recurrent hospitalisation** | | | | | | | | | | | | | | | |
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| LRTI | 12 | 47 | 35 | 357 | −74·7% (−88·2 to −45·9) | 14 | 35 | 21 | 595 | −62·4% (−79·6 to −30·9) | 26 | 101 | 75 | 167 | −75·5% (−85·2 to −59·4) |
| Acute bronchitis or bronchiolitis | 6 | 20 | 14 | 893 | −75·9% (−93·0 to −17·5) | 4 | 10 | 6 | 2082 | −76·9% (−94·4 to −5·3) | 10 | 39 | 29 | 431 | −81·6% (−92·4 to −55·2) |
| Pneumonia | 1 | .. | .. | .. | NC | 2 | .. | .. | .. | NC | 3 | .. | .. | .. | NC |
| All-cause | 257 | 363 | 106 | 118 | −29·0% (−41·7 to −13·6) | 155 | 168 | 13 | 961 | −7·4% (−27·9 to 19·0) | 538 | 642 | 104 | 121 | 16·0% (−27·8 to −2·3) |

Razzini JL, *et al*. Lancet Infect Dis. 2026:S1473-3099(25)00742-X

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Obs | Exp | Av | NNI | Relative change | Obs | Exp | Av | NNI | Relative change | Obs | Exp | Av | NNI | Relative change |
| **First primary health-care visit** | | | | | | | | | | | | | | | |
| Acute bronchitis or bronchiolitis | 1784 | 2577 | 793 | 16 | −30·8% (−41·9 to −17·5) | 1971 | 1535 | −436 | −28 | 28·5% (14·4 to 44·3) | 4297 | 4546 | 249 | 51 | −5·5% (−16·3 to 6·7) |
| Wheezing or asthma | 2267 | 3134 | 867 | 15 | −27·7% (−38·5 to −14·9) | 2292 | 1777 | −515 | −24 | 29·0% (16·3 to 43·0) | 5345 | 5572 | 227 | 56 | −4·0% (−13·9 to 7·0) |
| LRTI | 1879 | 2821 | 942 | 14 | −33·4% (−43·4 to −21·6) | 2120 | 1646 | −474 | −26 | 28·7% (15·2 to 43·9) | 4595 | 4961 | 366 | 35 | −7·3% (−17·7 to 4·3) |
| Respiratory infections | 4852 | 5115 | 263 | 48 | −5·2% (−13·2 to 3·6) | 2503 | 2177 | −326 | −38 | 15·1% (4·4 to 26·9) | 9471 | 9149 | −322 | −38 | 3·5% (−3·2 to 10·6) |
| Acute otitis media | 740 | 784 | 44 | 284 | −5·6% (−18·3 to 9·2) | 2370 | 2110 | −260 | −48 | 12·3% (2·6 to 22·8) | 3999 | 3743 | −256 | −48 | 6·9% (−0·7 to 15·2) |
| All otitis | 789 | 824 | 35 | 357 | 4·1% (−10·2 to 16·5) | 2411 | 2161 | −250 | −49 | 11·6% (2·1 to 22·0) | 4148 | 3862 | −286 | −43 | 7·3% (−0·1 to 15·2) |
| **First recurrent primary health-care visit** | | | | | | | | | | | | | | | |
| Acute bronchitis or bronchiolitis | 134 | 283 | 149 | 84 | −52·5% (−62·6 to −39·7) | 396 | 394 | −2 | −6246 | 0·6% (−17·6 to 22·8) | 623 | 814 | 191 | 66 | −23·3% (−34·0 to −10·8) |
| Wheezing or asthma | 401 | 555 | 154 | 82 | −28·2% (−37·3 to −17·8) | 899 | 817 | −82 | −152 | 10·0% (−2·8 to 24·5) | 1572 | 1623 | 51 | 245 | −3·1% (−11·9 to 6·5) |
| LRTI | 220 | 418 | 198 | 64 | −47·3% (−57·2 to −35·3) | 596 | 543 | −53 | −235 | 9·3% (−8·8 to 30·8) | 953 | 1146 | 193 | 65 | −16·6% (−27·3 to −4·3) |
| Respiratory infections | 1937 | 2345 | 408 | 31 | −17·3% (−25·2 to −8·6) | 3345 | 2784 | −561 | −22 | 20·1% (10·7 to 30·3) | 6603 | 6222 | −381 | −32 | 6·1% (−0·7 to 13·4) |
| Acute otitis media | 25 | 31 | 6 | 2082 | −22·3% (−53·6 to 30·1) | 323 | 251 | −72 | −173 | 30·0% (9·8 to 54·0) | 412 | 338 | −74 | −168 | 19·8% (2·6 to 39·9) |
| All otitis | 37 | 52 | 15 | 833 | −29·2% (−54·8 to 11·1) | 452 | 342 | −110 | −113 | 32·8% (13·4 to 55·7) | 602 | 498 | −104 | −120 | 21·0% (5·2 to 39·1) |

Razzini JL, *et al*. Lancet Infect Dis. 2026:S1473-3099(25)00742-X

Eurosurveillance

# Two-season effectiveness of a single nirsevimab dose against RSV hospitalisation in healthy term-born infants: a population-based case–control study, Spain, October 2023 to March 2025

Olivier Núñez[1,2] , Juan Juaneda[3] , Montserrat Martinez-Marcos[4] , Enriqueta Muñoz Platón[5] , Eva Rivas Wagner[6] , María-Isolina Santiago-Pérez[7] , Virginia Álvarez Río[8] , Matilde Zornoza Moreno[9] , Ana Fernández Ibáñez[10] , Gisselle Perez Suarez[11] , Gorka Loroño Ortiz[12] , Nerea Egüés[2,13] , Belén Berradre Sáenz[14] , María de los Ángeles Cuesta Franco[15] , Susana Casado Cobo[16] , María Domínguez Padilla[17] , Daniel Castrillejo[18] , Ana Míguez Santiyán[3] , Luca Basile[4] , María Ángeles Rafael de la Cruz López[5] , Diana Sanabria Curbelo[6] , Olaia Pérez-Martínez[7] , M Jesús Rodríguez Recio[8] , Lourdes Duro Gómez[9] , María del Pilar Alonso Vigil[10] , Manuel Mendez Diaz[11] , Rosa Sancho[12] , Jesús Castilla[2,13] , Ana Carmen Ibáñez Pérez[14] , Noa Batalla Rebollo[15] , Lucía Sánchez Piorno[16] , Ninoska López Berrios[19] , Joaquín Lamas[20] , Carmen Olmedo[21] , Susana Monge[1,22,*] , Roberto Pastor-Barriuso[1,2,*] , the Nirsevimab Effectiveness Study Collaborators[23]

Nuñez O, *et al*. Euro Surveill. 2026;31(9):pii=2500593.

Two-season effectiveness of catch-up nirsevimab immunisation against hospitalisation for respiratory syncytial virus infection among healthy term-born children, Spain, October 2023–March 2025 (based on data from n = 2,039 children)

| | 2023/24 RSV season | | | | | | 2024/25 RSV season | | | | | | Both RSV seasons | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases | | Controls | | Effectiveness | | Cases | | Controls | | Effectiveness | | Cases | | Controls | | Effectiveness | |
| | Immunised | Total | Immunised | Total | % | 95% CI | Immunised | Total | Immunised | Total | % | 95% CI | Immunised | Total | Immunised | Total | % | 95% CI |
| **Overall** | | | | | | | | | | | | | | | | | | |
| Pragmatic[a] | 131 | 235 | 775 | 903 | 85.1 | 79.2 to 89.4 | 173 | 188 | 663 | 713 | 12.8 | −59.2 to 52.2 | 304 | 423 | 1,438 | 1,616 | 72.3 | 63.0 to 79.3 |
| Intention to treat[b] | 137 | 255 | 737 | 953 | 65.8 | 55.8 to 73.6 | 158 | 188 | 575 | 713 | −43.1 | −117 to 5.7 | 295 | 443 | 1,312 | 1,666 | 37.6 | 22.3 to 50.0 |
| Per protocol[c] | 137 | 241 | 737 | 865 | 77.6 | 69.6 to 83.5 | 158 | 173 | 575 | 625 | −7.7 | −87.9 to 38.3 | 295 | 414 | 1,312 | 1,490 | 63.7 | 52.4 to 72.2 |
| **Single RSV infection[d]** | | | | | | | | | | | | | | | | | | |
| Pragmatic[a] | 104 | 190 | 627 | 730 | 84.8 | 78.1 to 89.5 | 115 | 127 | 455 | 484 | 34.1 | −36.8 to 68.2 | 219 | 317 | 1,082 | 1,214 | 76.6 | 67.3 to 83.2 |
| Intention to treat[b] | 109 | 206 | 591 | 768 | 65.3 | 53.8 to 73.9 | 105 | 127 | 402 | 484 | −5.2 | −70.4 to 35.1 | 214 | 333 | 993 | 1,252 | 47.5 | 33.0 to 58.9 |
| Per protocol[c] | 109 | 195 | 591 | 694 | 77.4 | 68.4 to 83.8 | 105 | 117 | 402 | 431 | 25.5 | −44.6 to 61.6 | 214 | 312 | 993 | 1,125 | 69.0 | 58.1 to 77.0 |

Nuñez O, *et al*. Euro Surveill. 2026;31(9):pii=2500593.

Two-season effectiveness of at-birth nirsevimab immunisation against hospitalisation for respiratory syncytial virus infection among healthy term-born children, Spain, October 2023–March 2025 (based on data from n = 3,217 children)

| | 2023/24 RSV season | | | | | | 2024/25 RSV season | | | | | | Both RSV seasons | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases | | Controls | | Effectiveness | | Cases | | Controls | | Effectiveness | | Cases | | Controls | | Effectiveness | |
| | Immunised | Total | Immunised | Total | % | 95% CI | Immunised | Total | Immunised | Total | % | 95% CI | Immunised | Total | Immunised | Total | % | 95% CI |
| **Overall** | | | | | | | | | | | | | | | | | | |
| Pragmatic[a] | 239 | 334 | 1,215 | 1,286 | 86.6 | 81.4 to 90.4 | 294 | 328 | 1,171 | 1,269 | 25.7 | −9.6 to 49.6 | 533 | 662 | 2,386 | 2,555 | 69.9 | 61.8 to 76.2 |
| Intention to treat[b] | 236 | 339 | 1,167 | 1,288 | 79.2 | 72.6 to 84.3 | 291 | 328 | 1,146 | 1,269 | 1.4 | −46.5 to 33.7 | 527 | 667 | 2,313 | 2,557 | 59.0 | 48.8 to 67.1 |
| Per protocol[c] | 236 | 331 | 1,167 | 1,238 | 84.3 | 78.7 to 88.5 | 290 | 324 | 1,139 | 1,237 | 19.5 | −20.7 to 46.3 | 526 | 655 | 2,306 | 2,475 | 67.4 | 58.9 to 74.2 |
| **Single RSV infection[d]** | | | | | | | | | | | | | | | | | | |
| Pragmatic[a] | 193 | 275 | 998 | 1,060 | 86.3 | 80.6 to 90.3 | 179 | 202 | 727 | 780 | 41.9 | 7.5 to 63.6 | 372 | 477 | 1,725 | 1,840 | 75.3 | 67.7 to 81.1 |
| Intention to treat[b] | 191 | 280 | 960 | 1,062 | 79.8 | 72.9 to 85.0 | 176 | 202 | 706 | 780 | 19.9 | −29.3 to 50.3 | 367 | 482 | 1,666 | 1,842 | 66.1 | 56.5 to 73.5 |
| Per protocol[c] | 191 | 273 | 960 | 1,022 | 84.1 | 78.1 to 88.5 | 175 | 198 | 702 | 755 | 37.4 | −2.5 to 61.8 | 366 | 471 | 1,662 | 1,777 | 73.6 | 65.7 to 79.7 |

Nuñez O, *et al*. Euro Surveill. 2026;31(9):pii=2500593.

**What have we learnt from this study?**

Nirsevimab immunisation reduced RSV hospital admissions by 64% to 74% during the first two RSV seasons of life overall. Most of this benefit was due to the protection during the first season, when children are at higher risk and have been recently immunised, while its benefit during the second season was low or null.

**What are the implications of your findings for public health?**

The net benefit of nirsevimab immunisation across the first two seasons of life was high, with no shift in the burden of RSV to the second post-immunisation season, endorsing current recommendations. Some residual benefit may extend to the second season for children born and immunised in February and March, which could be factored in when considering to include these birth cohorts in the immunisation programme.

Nuñez O, *et al*. Euro Surveill. 2026;31(9):pii=2500593.


NDC 0006-5073-01
One 105 mg/0.7 mL single-dose
prefilled syringe
GTIN 00300065073019
SN
EXP
LOT
ENFLONSIA™
(clesrovimab-cfor) Injection
105 mg / 0.7 mL
For Intramuscular Use Only
This package does not contain a needle.
Must be administered by a healthcare provi
REFRIGERATE
Rx Only
ENFLONSIA™
(clesrovimab-cfor)
Injection
105 mg / 0.7 mL
For Intramuscular Use Only

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Clesrovimab for Prevention of RSV Disease in Healthy Infants

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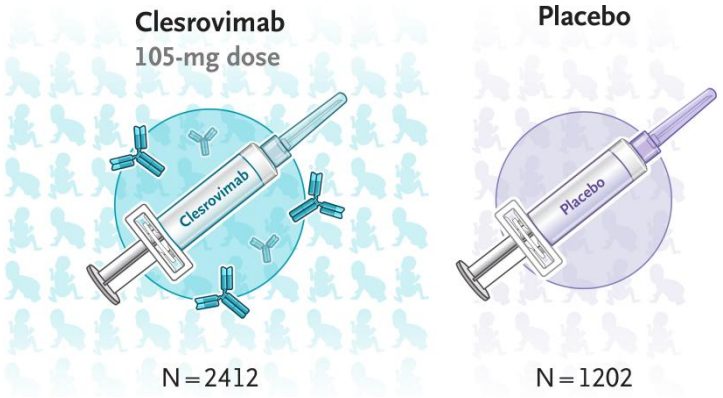
Zar HJ, *et al*. N Engl J Med. 2025;393(13):1292-1303.

## CLEVER [MK-1654-004]

**22 países**



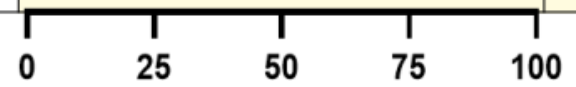
**<1 año sanos**
**(RNPT 29-34 sg, RNPT ≥35 sg y a término)**




Zar HJ, *et al*. N Engl J Med. 2025;393(13):1292-1303.

| RSV-Associated Endpoint[a] (Through 5 months) | Endpoint Designation | Efficacy through 5 months | | |
|---|---|---|---|---|
| | | Clesrovimab (n = 2,398) | Placebo (n = 1,201) | Observed Efficacy %, (95% CI) |
| | | # of Cases | # of Cases | |
| Severe MALRI | Tertiary | 2 | 12 | 91.7 (62.9, 98.1) |
| LRI Hospitalization | Tertiary | 5 | 27 | 90.9 (76.2, 96.5) |
| Hospitalization | Secondary | 9 | 28 | 84.2[d] (66.6, 92.6) |
| MALRI requiring ≥ 2 Indicators of LRI/Severity[b] | Post-Hoc | 10 | 41 | 88.0 (76.1, 94.0) |
| MALRI requiring ≥ 1 Indicator of LRI/Severity | Primary | 60 | 74 | 60.4[c] (44.1, 71.9) |
| Acute Respiratory Infection (ARI) | Tertiary | 148 | 148 | 52.0 (39.5, 61.9) |

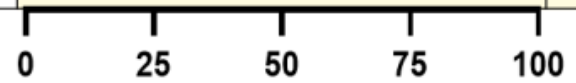
Increasing Disease Severity




https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/02-RSV-Mat-Peds-Sinha-508.pdf

| RSV-Associated Endpoint[a] *(Through 6 months)* | Endpoint Designation | Efficacy through 6 months | | |
|---|---|---|---|---|
| | | Clesrovimab (n = 2,398) | Placebo (n = 1,201) | Observed Efficacy %, (95% CI) |
| | | # of Cases | # of Cases | |
| Severe MALRI | Tertiary | 2 | 12 | 91.7 (62.9, 98.1) |
| LRI Hospitalization | Tertiary | 5 | 28 | 91.2 (77.2, 96.6) |
| Hospitalization | Tertiary | 11 | 29 | 81.3 (62.5, 90.7) |
| MALRI requiring ≥ 2 Indicators of LRI/Severity[b] | Post-Hoc | 11 | 42 | 87.2 (75.1, 93.4) |
| MALRI requiring ≥ 1 Indicator of LRI/Severity | Secondary | 64 | 77 | 59.5 (43.3, 71.1) |
| Acute Respiratory Infection (ARI) | Tertiary | 161 | 154 | 50.0 (37.4, 60.1) |

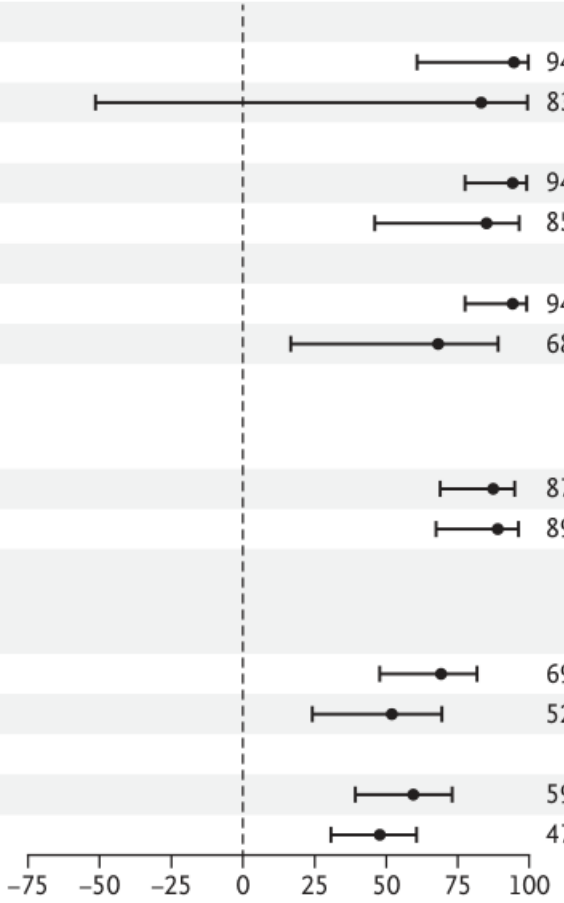
Increasing Disease Severity




https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/02-RSV-Mat-Peds-Sinha-508.pdf

**Figure 3.** Efficacy of Clesrovimab through 150 Days after Injection for RSV-Associated End Points, According to Body Weight at Randomization.

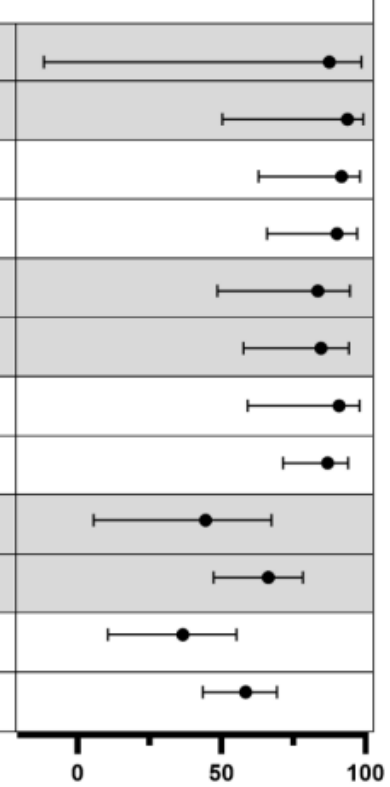
| RSV-Associated End Point, According to Body Weight at Randomization | Clesrovimab (<5 kg, N=860; ≥5 kg, N=1538) | Placebo (<5 kg, N=428; ≥5 kg, N=773) | Efficacy (95% CI) |
|---|---|---|---|
| | *no. of cases* | *no. of cases* | *percent* |
| Severe medically attended LRI | | | |
| <5 kg | 1 | 9 | 94.6 (60.8 to 99.7) |
| ≥5 kg | 1 | 3 | 83.3 (–51.4 to 99.4) |
| Hospitalization for LRI | | | |
| <5 kg | 2 | 17 | 94.3 (77.6 to 99.1) |
| ≥5 kg | 3 | 10 | 85.1 (46.1 to 96.5) |
| Hospitalization | | | |
| <5 kg | 2 | 17 | 94.3 (77.6 to 99.1) |
| ≥5 kg | 7 | 11 | 68.3 (16.8 to 89.2) |
| Medically attended LRI with ≥2 indicators of LRI or disease severity | | | |
| <5 kg | 6 | 23 | 87.4 (69.0 to 94.9) |
| ≥5 kg | 4 | 18 | 89.0 (67.5 to 96.3) |
| Medically attended LRI with ≥1 indicator of LRI or disease severity | | | |
| <5 kg | 23 | 36 | 69.3 (47.9 to 81.8) |
| ≥5 kg | 37 | 38 | 52.0 (24.3 to 69.6) |
| Acute respiratory infection | | | |
| <5 kg | 44 | 52 | 59.6 (39.3 to 73.1) |
| ≥5 kg | 104 | 96 | 47.8 (30.8 to 60.7) |




Zar HJ, *et al*. N Engl J Med. 2025;393(13):1292-1303.

Figure S4. Efficacy Through Days 1-150 by RSV A and B Subtype

| RSV-Associated Endpoint | RSV Subtype | Clesrovimab (n=2398) # of cases | Placebo (n=1201) # of cases | Efficacy (95% CI)[a] |
|---|---|---|---|---|
| Severe Medically Attended LRI | RSV A | 1 | 4 | 87.5 (-11.8, 98.6) |
| | RSV B | 1 | 8 | 93.8 (50.2, 99.2) |
| **Hospitalization for LRI** | **RSV A** | **2** | **12** | **91.7 (62.9, 98.1)** |
| | **RSV B** | **3** | **15** | **90.1 (65.7, 97.1)** |
| Hospitalization | RSV A | 4 | 12 | 83.4 (48.5, 94.6) |
| | RSV B | 5 | 16 | 84.5 (57.6, 94.3) |
| **Medically Attended LRI with ≥ 2 Indicators of LRI/ Severity** | **RSV A** | **2** | **11** | **90.9 (59.1, 98.0)** |
| | **RSV B** | **8** | **30** | **86.9 (71.3, 94.0)** |
| Medically Attended LRI with ≥ 1 Indicator of LRI/ Severity | RSV A | 29 | 26 | 44.4 (5.5, 67.3) |
| | RSV B | 33 | 48 | 66.2 (47.2, 78.3) |
| **Acute Respiratory Infection** | **RSV A** | **74** | **58** | **36.6 (10.5, 55.2)** |
| | **RSV B** | **78** | **91** | **58.4 (43.5, 69.3)** |




Zar HJ, *et al*. N Engl J Med. 2025;393(13):1292-1303.

Figure S5. Efficacy Through Days 1-150 by Gestational Age Subgroups

| RSV-Associated Endpoint | Gestational Age, Weeks | Clesrovimab # of cases/ number eligible[a] | Placebo # of cases/ number eligible[a] | Efficacy (95% CI) [b] |
|---|---|---|---|---|
| Severe Medically Attended LRI | ≥29 to <35 | 1/417 | 4/208 | 87.7 (5.6, 99.5) |
| | ≥35 | 1/1981 | 8/993 | 93.8 (60.3, 99.7) |
| **Hospitalization For LRI** | **≥29 to <35** | **1/417** | **10/208** | **95.2 (67.6, 99.8)** |
| | **≥35** | **4/1981** | **17/993** | **88.3 (66.8, 96.4)** |
| Hospitalization | ≥29 to <35 | 3/417 | 11/208 | 86.8 (52.6, 96.3) |
| | ≥35 | 6/1981 | 17/993 | 82.5 (55.6, 93.1) |
| **Medically Attended LRI with ≥ 2 Indicators of LRI/ Severity** | **≥29 to <35** | **3/417** | **13/208** | **88.9 (63.1, 97.3)** |
| | **≥35** | **7/1981** | **28/993** | **87.7 (71.4, 95.1)** |
| Medically Attended LRI with ≥ 1 Indicators of LRI/ Severity | ≥29 to <35 | 9/417 | 21/208 | 79.8 (55.5, 90.8) |
| | ≥35 | 51/1981 | 53/993 | 52.6 (30.3, 67.8) |
| **Acute Respiratory Tract Infection** | **≥29 to <35** | **27/417** | **30/208** | **57.9 (28.4, 75.3)** |
| | **≥35** | **121/1981** | **118/993** | **50.5 (36.0, 61.7)** |

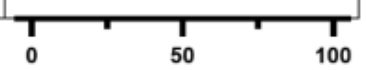



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**Table 2.** Adverse Events (Safety Population).*

| Adverse Event | Clesrovimab (N=2409) | Placebo (N=1202) | Estimated Difference (95% CI)† |
|---|---|---|---|
| | *no. of infants (%)* | | *percentage points* |
| Overall adverse events‡ | | | |
| Any adverse event | | | |
| ≥1 Adverse event | 1816 (77.3) | 932 (77.5) | −0.3 (−3.1 to 2.7) |
| Related to clesrovimab or placebo | 696 (28.9) | 344 (28.6) | 0.3 (−2.9 to 3.4) |
| Any serious adverse event | 278 (11.5) | 149 (12.4) | −0.9 (−3.2 to 1.3) |
| Related to clesrovimab or placebo | 1 (<0.1) | 1 (0.1) | 0.0 (−0.4 to 0.2) |
| Death§ | 7 (0.3) | 3 (0.2) | 0.0 (−0.5 to 0.4) |
| Solicited adverse event or fever on days 1–5 after injection | | | |
| Injection-site reaction | 274 (11.4) | 141 (11.7) | −0.4 (−2.6 to 1.8) |
| Erythema | 107 (4.4) | 43 (3.6) | 0.9 (−0.6 to 2.2) |
| Pain | 156 (6.5) | 96 (8.0) | −1.5 (−3.4 to 0.2) |
| Swelling | 77 (3.2) | 38 (3.2) | 0.0 (−1.3 to 1.2) |
| Solicited systemic adverse event | 726 (30.1) | 375 (31.2) | −1.1 (−4.3 to 2.1) |
| Decreased appetite | 131 (5.4) | 73 (6.1) | −0.6 (−2.3 to 0.9) |
| Irritability | 517 (21.5) | 264 (22.0) | −0.5 (−3.4 to 2.3) |
| Somnolence | 333 (13.8) | 192 (16.0) | −2.2 (−4.7 to 0.3) |
| With fever | 13 (0.5) | 14 (1.2) | −0.6 (−1.4 to −0.0) |
| Adverse event of special interest on days 1–42 after injection | | | |
| Anaphylaxis or hypersensitivity | 1 (<0.1) | 0 | 0.0 (−0.3 to 0.2) |
| Rash | 11 (0.5) | 4 (0.3) | 0.1 (−0.4 to 0.5) |

Zar HJ, *et al*. N Engl J Med. 2025;393(13):1292-1303.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

# Clesrovimab in Infants and Children at Increased Risk for Severe RSV Disease

Zar HJ, *et al*. N Engl J Med. 2025;393(13):1343-1345.

# SMART [MK-1654-007]

Diverse population enrolled
from **27 countries or territories**



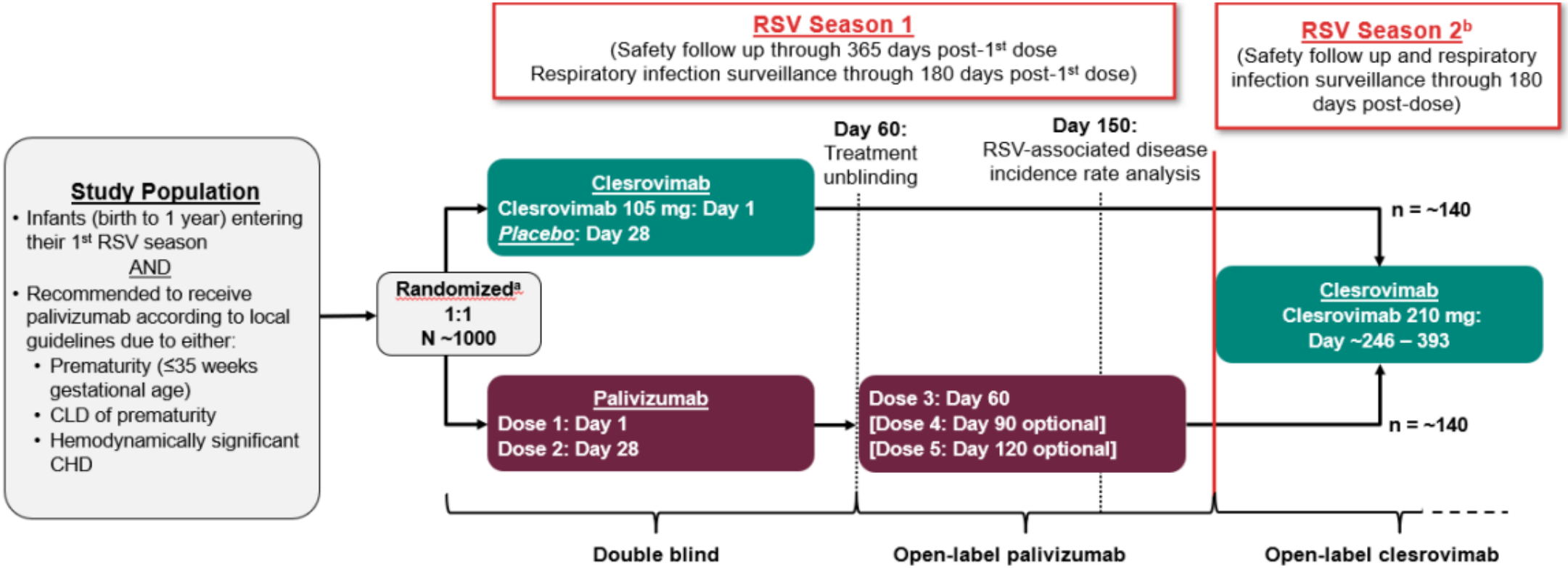
**<1 año de riesgo**
**(RNPT <29 sg, RNPT 29-34 sg, enfermedad pulmonar crónica o cardiopatía hemodinámicamente significativa)**

| | Clesrovimab 105 mg | | Palivizumab | | Total | |
|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | n | (%) |
| Participants randomized | 450 | | 451 | | 901 | |
| Participants included in analyses | 443 | (98.4) | 437 | (96.9) | 880 | (97.7) |

Zar HJ, *et al*. N Engl J Med. 2025;393(13):1343-1345.

**Figure S1: SMART Trial (MK-1654-007) Design**

Phase 3, randomized, partially-blinded, active comparator-controlled trial evaluating the safety, tolerability and incidence rates of RSV-associated disease after administration of clesrovimab compared to palivizumab in infants and children at increased risk for severe RSV Disease




https://www.nejm.org/doi/suppl/10.1056/NEJMc2506107/suppl_file/nejmc2506107_appendix.pdf

**Table 1.** Adverse Events during RSV Season 1.*

| Adverse Event | Clesrovimab (N=445) | Palivizumab (N=450) | Estimated Difference (95% CI)† |
|---|---|---|---|
| | *number of infants (percent)* | | *percentage points* |
| **All adverse events** | | | |
| Any adverse event | | | |
| ≥1 Adverse event | 335 (75.3) | 358 (79.6) | −4.3 (−9.8 to 1.2) |
| Drug-related‡ | 141 (31.7) | 163 (36.2) | −4.5 (−10.7 to 1.7) |
| Serious adverse events | | | |
| Any | 99 (22.2) | 112 (24.9) | −2.6 (−8.2 to 2.9) |
| Drug-related‡ | 0 | 2 (0.4) | −0.4 (−1.6 to 0.4) |
| Death§ | 8 (1.8) | 4 (0.9) | 0.9 (−0.7 to 2.7) |
| **Solicited adverse events or fever** | | | |
| Injection-site adverse events | 69 (15.5) | 76 (16.9) | −1.4 (−6.2 to 3.5) |
| Erythema | 31 (7.0) | 27 (6.0) | 1.0 (−2.3 to 4.3) |
| Pain | 35 (7.9) | 51 (11.3) | −3.5 (−7.4 to 0.4) |
| Swelling | 29 (6.5) | 24 (5.3) | 1.2 (−2.0 to 4.4) |
| Systemic adverse events | 180 (40.4) | 195 (43.3) | −2.9 (−9.3 to 3.6) |
| Decreased appetite | 59 (13.3) | 59 (13.1) | 0.1 (−4.3 to 4.6) |
| Irritability | 133 (29.9) | 154 (34.2) | −4.3 (−10.4 to 1.8) |
| Somnolence | 88 (19.8) | 103 (22.9) | −3.1 (−8.5 to 2.3) |
| With fever | 4 (0.9) | 6 (1.3) | −0.4 (−2.1 to 1.1) |
| **Adverse events of special interest** | | | |
| Anaphylaxis or hypersensitivity | 0 | 0 | 0.0 (−0.8 to 0.9) |
| Rash | 3 (0.7) | 1 (0.2) | 0.5 (−0.6 to 1.8) |

**Table 2.** Incidence of RSV-Associated Secondary End Points in RSV Season 1.*

| End Point† | Clesrovimab (N=443) | | | Palivizumab (N=437) | | |
|---|---|---|---|---|---|---|
| | No. of Cases | Total Follow-up Time | Incidence over 5 Months (95% CI)‡ | No. of Cases | Total Follow-up Time | Incidence over 5 Months (95% CI)‡ |
| | | *mo* | % | | *mo* | % |
| Medically attended lower respiratory infection with ≥1 indicator of lower respiratory infection or disease severity | 14 | 1946.9 | 3.6 (2.0–6.0) | 12 | 1969.5 | 3.0 (1.6–5.3) |
| Hospitalization | 5 | 1968.9 | 1.3 (0.4–3.0) | 6 | 1987.3 | 1.5 (0.6–3.3) |

Zar HJ, *et al*. N Engl J Med. 2025;393(13):1343-1345.

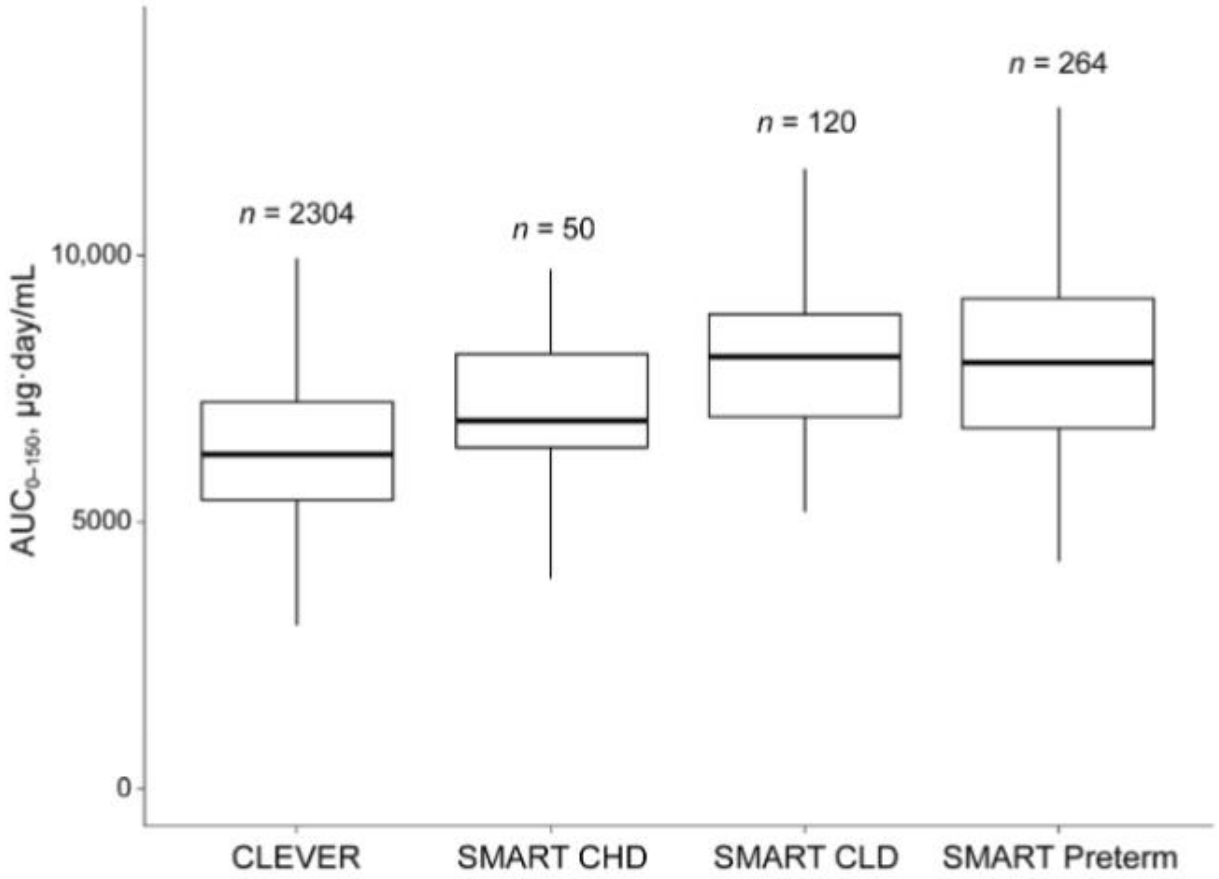



**Figure 4** Comparison of $AUC_{0-150}$ for infants in CLEVER vs. risk subgroups in SMART season 1 based on popPK analysis. $AUC_{0-150}$, area under the concentration–time curve over the first 150 days; CHD, congenital heart disease; CLD, chronic lung disease; popPK, population pharmacokinetics.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