RSV Prophylaxis With Nirsevimab in Infants: Systematic Review of Early Real-World Evidence on Effectiveness and Impact

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BACKGROUND

- Respiratory syncytial virus (RSV) is a leading cause of respiratory tract infections and hospitalisations among infants worldwide, with almost all children experiencing an RSV infection by the time they are 3 years old[1-6]
- RSV thus represents a significant public health burden, particularly in the first year of life[6-9]
- In order to address this unmet need and provide RSV protection to all infants regardless of risk factors present, the extended half-life monoclonal antibody nirsevimab was developed and introduced beginning in 2023 as a single-dose immunisation available to all infants[10-13]
- This systematic review aims to summarise early real-world evidence on achieved immunisation rates and evaluate the impact and effectiveness of nirsevimab prophylaxis on infants

METHODS

Search criteria

- A systematic literature search for full-text publications following PRISMA guidelines was conducted in the databases PubMed and Embase for articles published from 2023-2024
- The search utilised MeSH (PubMed) and Emtree (Embase) terms to identify articles linking RSV or RSV infections, the population of infants and young children, and antibody or nirsevimab intervention. An exploratory manual search was also carried out
- Given that the introduction of nirsevimab was recent, the initial search from March 26, 2024, was repeated on May 28, 2024, and September 11, 2024
- Study inclusion criteria:
  - Observational studies investigating nirsevimab in routine use (i.e., real-world evidence, or RWE)
  - Relevant topics reporting on public health impact: Immunisation rates, nirsevimab effectiveness, and changes in hospitalisation incidence or other health care resource utilisation

RESULTS

Search results

- 49 articles for full-text review were identified based on an initial screen of the title/abstract and were screened for relevance based on the inclusion/exclusion criteria
- This process identified 8 articles in the original search, and after the refreshed searches, a final database of 20 observational articles to analyse (**Supplemental Figure 1, see QR code**)
  - Geographically, the articles were distributed across Spain,[14-25] Andorra,[23] France,[26-30] Luxembourg,[31] Italy,[32] and the United States[33] (**Figure 1**)
  - Studies included 7 case-control, 5 prospective, 3 ecological, 3 retrospective, and 2 ambispective cohort studies

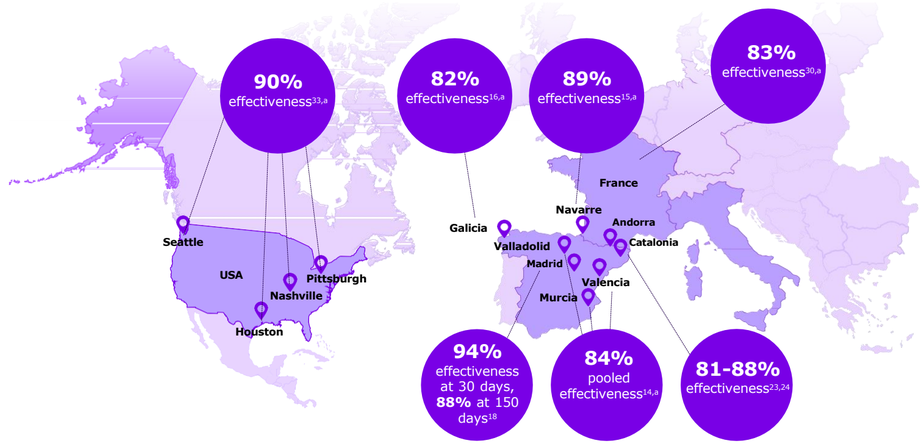
Immunisation rate

- Nirsevimab had been introduced in all regions by Fall 2023 (with the exception of the Italian region Valle d'Aosta, where it became available in December 2023,[32] and Andorra, where it became available in early 2024[23] (**Figure 2**)
- 10 studies from Spain, the Catalonia region, Andorra, Luxembourg, and Italy reported immunisation rates for nirsevimab, with overall immunisation rates ranging from 60-99% (**Figure 2**, lower bound from the Andorra region where it was introduced later)

Public health impact

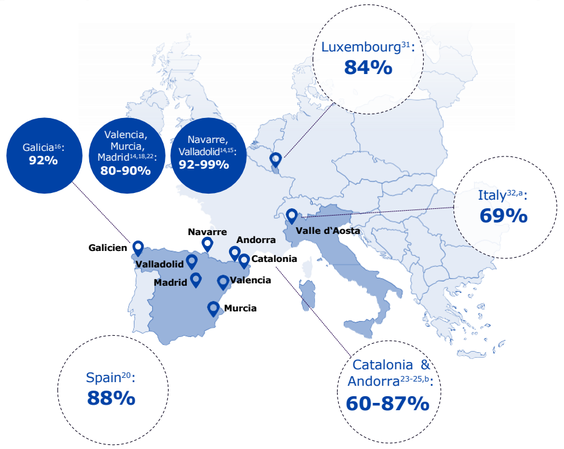
- The effectiveness of nirsevimab in preventing RSV-associated hospitalisations ranged from 81-94% (**Figure 1**)
- Nirsevimab further provided protection against RSV-related hospitalisation burden (**Figure 3**), severe RSV infection, ED visits, and ICU stays:
  - In Spain, nirsevimab was effective in preventing emergency care (67%), hospital admissions (88%), and ICU stays (68-94%)[18,21,24,25]
  - The Catalonia and Andorra region reported 86% effectiveness at preventing severe infection (need for NIV/CMV)[23]
  - In France, nirsevimab was 70% effective at preventing critical care,[27] 76% effective against severe cases of RSV-related bronchiolitis,[29] 83% effective against ED visits for RSV-associated bronchiolitis, and 91% effective at reducing need for supplemental oxygen[30]

Figure 1: Effectiveness of nirsevimab in preventing LRTI-related hospitalisations due to RSV, based on international RWE



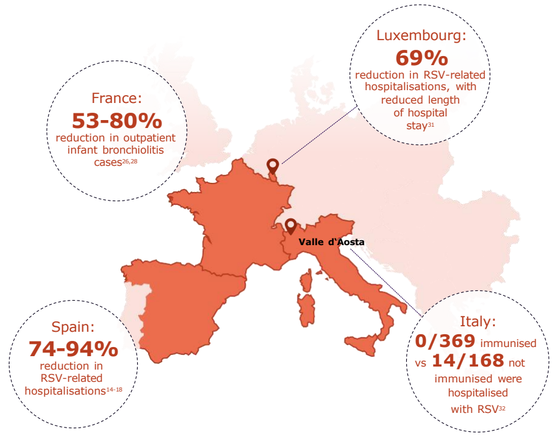
[a]In the prevention of LRTI-related hospitalisations due to RSV.

Figure 2: Reported nirsevimab immunisation rates at time of analysis



[a]Immunisation program implemented in December 20, 2023.
[b]Immunisation program implemented in October 2023 in Catalonia and in 2024 in Andorra.

Figure 3: Impact of nirsevimab in reducing RSV-related burden



RESULTS (CONTINUED)

- Spain (Valencia) reported 74% effectiveness at preventing RSV infection in immunised individuals, with lower incidence of hospitalisations 0.9% (218/24,233) with nirsevimab compared to 1.6% (49/3,139) without nirsevimab immunisation[22]
- In Luxembourg, average length of stay in the hospital was reduced from 5.6 days in the 2022-2023 season to 3.4 days in the 2023-2024 season for infants <6 months of age[31]
- The Catalonia and Andorra region reported 99% effectiveness at preventing hospitalisation due to RSV in premature infants (<36 weeks)[23]
- France saw a 53-80% reduction in the number of outpatient infant bronchiolitis cases[26,28]

Safety results

- Safety data were reported in 3 studies, with 2 of the 3 studies reporting no occurrence of adverse events (AEs)[15,31]
  - In the 1 study reporting mild side effects, 11% of recipients reported AEs, including fever, local reactions, and barely consolable crying, all of which occurred within 2 weeks of administration and generally appeared within 48 hours, lasting only 1-2 days[32]
- No serious adverse events were reported in the included publications

LIMITATIONS

- Observational studies can underestimate the effectiveness of prevention because of potential errors in RSV testing in the real-world clinical setting, or because of confounding errors due to misclassification of data
- The varying inclusion criteria across studies included in this publication set should be considered, as well as the generalisability of data within the reference set in the context of potential regional differences in the circulation of RSV, or differences in how much of the RSV season was covered across study evaluation periods
- A formal bias analysis was not conducted on these data

CONCLUSIONS

- **With the advent of the monoclonal antibody nirsevimab in 2023, it is now possible to provide widespread protection against RSV with the adoption of population-wide immunisation of infants across regions**
- **Consistently high effectiveness of nirsevimab has been observed in real-world settings**
- **The public health impact of nirsevimab has been demonstrated with strong reductions in RSV-related hospitalisations**

ABBREVIATIONS

CMV, conventional mechanical ventilation; ED, emergency department; HCRU, health care resource utilisation; ICU, intensive care unit; LRTI, lower respiratory tract infection; NIV, noninvasive mechanical ventilation; RSV, respiratory syncytial virus; RWE, real-world evidence; US, United States.

DISCLOSURES

- MW, ACM, OD, AW, OM, and RK are Sanofi employees and may hold shares and/or stock options in the company. MK has been Head of Clinical Trial (LKP) / Principal Investigator (PI) in vaccine clinical trials and participated in advisory boards of GSK, Pfizer, and Sanofi as part of employment responsibilities.

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References are available on the electronic version by scanning the QR code.

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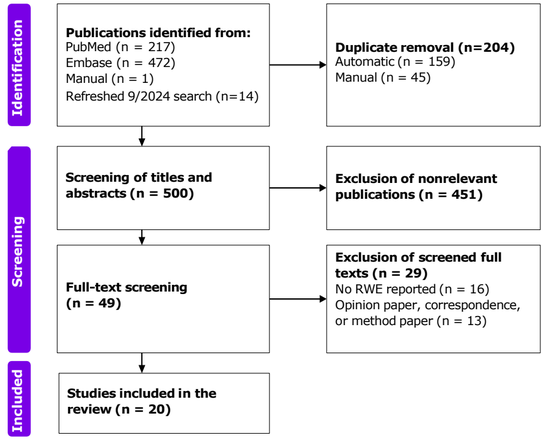
Supplemental Figure 1: Flowchart of the identification and publication selection process



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