Impact of Nirsevimab on Admission to Pediatric Intensive Care Unit because of RSV Bronchiolitis: unicentric observational study from 2017-2024

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To the editor,

Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract infections (LRTI) in children. Also, is the principal cause of acute bronchiolitis (AB), which have a considerable impact on the healthcare system and later comorbidities[1].

In the last years, there has been different immunological approaches to prevent RSV infection: passive immunization through antibodies administration; maternal vaccination during pregnancy; or active immunization of infants. Nirsevimab (Beyfortus, AstraZeneca/Sanofi Pasteur) is one example of passive immunization[2]. This monoclonal antibody against RSV, with around six-month effect, has shown potential in preventing RSV-LRTI hospital admission.

In Spain, passive immunization with Nirsevimab was initiated in late September 2023 for all infants born from 1 April 2023. This decision was controversial from a cost-effectiveness point of view[1]. Nowadays, there is scarce real-world clinical data about Nirsevimab impact over RSV-related hospitalisations[3]. Also, the possible influence on pediatrical critical care unit (PICU) admissions has not been described[4].

In this brief report, we analyse the PICU admissions because of AB-RSV in 2023-2024 in a monographic pediatric centre. Later, we compare this data with the six previous years to define epidemiological differences.

We made a prospective-retrospective observational study (October 2017-February 2024). It was conducted on children admitted to PICU because of AB by RSV. Epidemiological data were collected. Patients were grouped into "typical" epidemic waves (TEW, those occurring from November to March) or "atypical" waves (AEW, from April to October). Groups were compared using statistical tests according to the collected variables, considering significance $p<0.05$. Quantitative variables were expressed as mean, median, and interquartile range (IQR).

In 2023-2024, 21 patients were recruited, out of which 19/21 were RSV; 3/19 had received Nirsevimab. Children RSV positive without Nirsevimab had a median age of 140,4 days (RI 184) and those with Nirsevimab age of 76 days (RI 41). Significative differences were not observed. There were 12/21 males with a median age of 114 days (IQR 174) and a median length of stay of 3 days (IQR 2). Related to those with RSV 12/19 were males.

A total of 435 admissions for AB in the PICU were analysed. Their RSV diagnosis, age at admission and days of PICU treatment are described in supplemental **Table 1** .

Nine epidemic RSV waves were observed. Two AEWs: 1) 2021: 41/370, 2) 2022: 22/370. Seven TEWs with the following admissions: 1) 2017-2018: 53/370, 2) 2018-2019: 64/370, 3) 2019-2020: 68/370, 4) 2020-2021: 1/370, 5) 2021-2022: 35/370, 6) 2022-2023: 65/370, 7) 2023-2024: 22/370. To avoid bias the atypical epidemic waves occurring during the pandemic were excluded from the comparison analysis (see Figure 1). The mean of PICU RSV admission per wave prior to Nirsevimab was 62.5 ($\pm$6.5). In 2023-204 was observed a 68% decrease ($p<0.05$). Also, 2023-2024 positive RSV children were older than those from 2018-2019 (p=0,045) and 2022-2023 (p=0,011).

In our series, we observed a low number of admissions due to BA-RSV during the 2023-2024 season. The majority of them caused by RSV and in patients who have not received Nirsevimab. From an epidemiological perspective, they showed a higher median age than previous years. Compared to previous epidemic seasons, we describe a clear decrease in the number of BA-RSV cases.

Currently, there is scarce real-world evidence regarding the impact of Nirsevimab. A study published in Spain appears to demonstrate an effectiveness of at least 70% in preventing hospital admissions[5]. However, the impact on critically ill patients is not completely described[3]. So, this report is the first to provide such information.

We also observe a change in the age profile of RSV patients. This could be another indirect data about the impact of the passive immunization. This phenomenon has already been described in France[6]. We observed differences with two of the four non pandemic waves analysed. We did not compare the clinical complexity between waves, this should be considered in future studies.

In the next years, the possible immune effect of Nirsevimab on RSV reinfection should be monitorized. Also, epidemiological modifications linked to viral competition derived from the new clinical scenario must be analysed. The infection dynamic followed by RSV and other viruses will be of great interest to understand it.

This brief report has limitations. It was conducted in a single centre. While this ensures homogeneity on diagnostic and clinical management, it does not eliminate possible biases related to patient characteristics. Also, it may only represent the epidemiological situation of a specific geographical location. A strength of our observations is the inclusion of pre-pandemic years. The incorporation of three epidemic waves unaffected by public health measures related to SARS-CoV-2 allows to obtain more accurate observations.

In conclusion, we observed that the majority of PICU admissions because of RSV-BA during the period 2023-2024 did not received Nirsevimab. Additionally, a decrease of cases was observed when considering

previous non-pandemic epidemics. These observations should be confirmed with data from other centres and future epidemic waves.

Figure 1. PICU acute bronchiolitis admissions included in the analysis. Separated based on positive or negative RSV.

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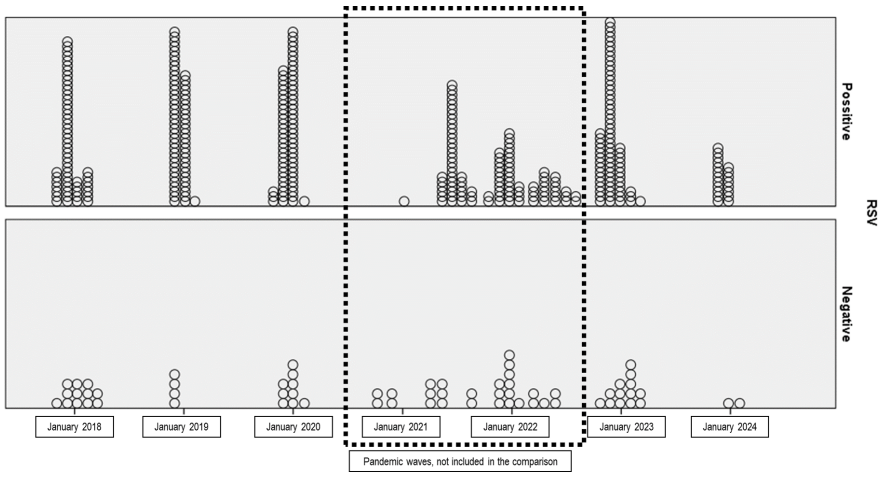

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`Table 1.docx` available at https://authorea.com/users/781697/articles/936143-impact-of-nirsevimab-on-admission-to-pediatric-intensive-care-unit-because-of-rsv-bronchiolitis-unicentric-observational-study-from-2017-2024