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Nirsevimab: Reducing RSV Infections in Infants

Nirsevimab, an monoclonal antibody for the prevention of RSV infection, will now be available for administration to infants from this autumn. It works by preventing the virus entry into the host cell by binding the F1 and F2 subunits of the RSV fusion (F) protein.

The Randomised Control Trials and real world clinical experience have found that it is very effective in preventing infant hospitalisation from RSV infection. A single dose of Nirsevimab has demonstrated a sustained and consistent reduction in RSV respiratory tract infections in infants. It is well tolerated with a favourable safety profile. Side effects reported from the trials have been minor with injection site reaction 0.3%, and rash within 14 days 0.9%. Nirsevimab has an extended half life greater than 3 times that of typical monoclonal antibodies. One dose is sufficient to cover 150 days, the entire RSV season.

It was approved by the EMA (European medicines agency) in October 2022, Canada April 2023, USA July 2023. NIAC (national immunisation advisory committee) on 12/10/23 recommended the passive immunisation of all infants against RSV during their first RSV season.

RSV is highly infectious. The typical clinical picture is runny nose, cough, wheezing, mild temperature, and poor feeding. In more severe cases the added features include tachypnoea, grunting, chest retractions, cyanosis out of oxygen, and apnoec spells.
It is the leading cause of hospital admission in young infants during the winter months. The RSV season extends between September and February, the rate of new cases peaking in week 45 (Nov 4-10). The number of RSV hospitalisations[1] in children less than 2 years was 2,727 in 2022, the preponderance being young infants.

There have been a number of key trials demonstrating the efficacy of Nirsevimab. The MELODY trial[2] reported on March 2, 2022. It involved 1490 term and near term infants randomised to Nirsevimab or placebo on a 2:1 ratio. The number of medically attended RSV infections was - 12/994 (1.2%) of infants in the Nirsevimab limb developed RSV compared with 25/496 (5%) in the control limb. The efficacy being 74.5%.

The HARMONIE trial[3] reported on Dec 27,2023. It included infants from 29 weeks gestation. The primary end point was hospitalisation with RSV. There were 8058 infants randomised to either Nirsevimab or placebo. 11/4037 (0.27%) were hospitalised with RSV in the Nirsevimab group and 60/4021 (1.49%) infants in the control group. The efficacy was 83.2%.

The MEDLEY trial[4] compared Nirsevimab and Palivizumab among RSV high risk infants- preterm <35 weeks, chronic lung disease of infancy (CLD), and infants with congenital heart disease. It was a 2:1 study with the infants being randomised to either Nirsevimab 50mg one dose vs 5 doses of Palivizumab 15mg/kg. The number of cases of RSV through 150 days was 4/616 (0.6%) in the Nirsevimab infants and 3/309 (1.6%) in the Palivizumab infants.

The use of Nirsevimab in Galacia, Spain, the NIRSE Gal study[5] reported on Dec 27, 2023. A total of 9408 of 10,259 eligible infants received Nirsevimab, which represents a 91.7% uptake. In previous RSV seasons (2016-23) prior to the introduction of Nirsevimab, 3-5 infants out of every 100 were hospitalised with RSV. Nirsevimab in its first year resulted in an 82% reduction in RSV hospitalisations.

The picture that emerges is that Nirsevimab leads to an 80% reduction in RSV hospitalisations in infants. It has the potential to substantially reduce the morbidy associated with RSV each winter. It will alleviate the seasonal pressures on paediatric units throughout the country. The NNT (number needed to treat) to prevent a hospitalisation is 25.

A working group was established by the CCO. It recommended the introduction of a pathfinder programme for infants born during this coming RSV season. The Minister of Health announced on June 18, 2024 that funding has been made available for the administration of Nirsevimab to all infants born in Ireland during the six months (September '24 – February '25). A Pathfinder Programme refers to a strategic initiative designed to explore innovative approaches to improving health outcomes within a community or population. These programmes often serve as pilots or models that, if successful, can be scaled up and replicated in other settings.

A pathfinder programme steering group has been established by Public Health: National Health Protection Office and Access and Integration to oversee the programme. Other agencies including HSE, midwives, NWIHP, the faculty of paediatrics, and hospital pharmacists have been involved.

It will be administered across all maternity hospitals prior to the infant's discharge home.
The Nirsevimab dose is 50mg (0.5 mls) for all infants birthweight <5 Kg and 100 mg (1 ml) for infants >5Kg. It is supplied in prefilled syringes. It is stored in a fridge, 2 C -8 C. It may be kept at room temperature for up to 8 hours. It is administered by IM injection into the antero-lateral aspect of the thigh.

Nirsevimab offers the potential to significantly reduce the number of infants acquiring RSV infection each winter.

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