NNF position statement on Palivizumab for RSV prophylaxis

Purpose of the position statement

Palivizumab, a monoclonal antibody, has recently been licensed in India. The NNF position statement aims to provide recommendations to optimize drug use in a suitable population.

Respiratory Syncytial virus

Respiratory Syncytial virus (RSV) is a major cause of acute respiratory infections requiring hospital admissions in infants, the majority of cases occurring in infants less than 6 months of age.

Prematurity, Bronchopulmonary dysplasia, babies with congenital heart disease, post tracheostomy, Cystic fibrosis, Congenital immunodeficiency, and neuromuscular disorders are associated with increased risk for severe RSV infections.

Prevention

RSV treatment options are only supportive, and prevention is the most effective strategy. A preventive strategy against serious RSV infections is administering antenatal RSV vaccine and postnatal monoclonal antibodies. Palivizumab and Nirsevimab are monoclonal antibodies recommended for postnatal RSV prophylaxis. Recently, Palivizumab has been made available in India.

RSV season

RSV infections in developed countries show a seasonal trend. There is limited information on RSV season in India; recent studies from India have shown an increased incidence of RSV from July to November, with a smaller peak during December, January, and February.

Palivizumab

Palivizumab is a recombinant humanized immunoglobulin (IgG1) monoclonal antibody. Administration of palivizumab provides passive immunity against RSV.

Mode of action

After intramuscular administration, Palivizumab is distributed hematogenously throughout the body, including the lower respiratory tract. When RSV encounters palivizumab in the lower respiratory tract, the antibody binds to the F protein and prevents the structural conformational change that is necessary for the fusion of the viral RSV envelope with the plasma membrane of the respiratory epithelial cell. Without fusion, the virus cannot enter the cell or replicate. In addition, palivizumab prevents cell-to-cell fusion of RSV-infected cells.

Palivizumab is recommended

- Babies born at less than 29 weeks until 12 months of age.
- Babies >29 -32 weeks with bronchopulmonary dysplasia (BPD) (defined as the need for oxygen at 36 weeks of corrected gestation)
- Babies with congenital heart disease (CHD) are at risk of congestive heart failure or on anti-failure medications, awaiting cardiac surgery, or CHD with moderate to severe PAH.

Palivizumab may be considered

In babies with cystic fibrosis, post-tracheostomy, and immunocompromised babies.

Palivizumab is contraindicated

- An absolute contraindication of Palivizumab in patients with known hypersensitivity to palivizumab or any of its excipients or other humanized monoclonal antibodies.
- Palivizumab injection should be administered with caution to patients with thrombocytopenia or any coagulation disorder.
- Palivizumab may not be deferred in a mild febrile illness such as upper respiratory tract infection; however, it may be deferred in moderate to severe infection or febrile illness.

Who should not receive Palivizumab?

- There is no evidence to support the use of palivizumab to prevent healthcare-associated infection in neonates. Emphasis should be laid on infection control practices and hand hygiene.
- There is no role of palivizumab in the treatment of RSV-infected children. Although there may be a reduction of RSV viral load with the use of palivizumab, this does not translate into therapeutic benefits or alteration of disease severity[i].

Dose

The dose is 15 mg/kg, once per month for 5 months; 15 mg/kg/dose has been shown to achieve a mean trough serum concentration that is associated with a 99% reduction of RSV.

Palivizumab and vaccination schedule

Childhood immunization schedules should be followed irrespective of the use of palivizumab. Palivizumab and scheduled vaccines can be administered simultaneously at separate sites.

RSV prophylaxis following RSV infection

Infants and children who develop an RSV infection while receiving palivizumab should continue to receive prophylaxis after recovery from their acute infection.

RSV is classified into subgroups A and B based on antigenic differences in the surface G glycoprotein. Subgroups are classified further into genotypes based on genetic analysis. The ability of RSV to cause reinfections throughout life is likely attributable to strain variability and an immune response that does not fully protect against subsequent infection. Reinfections with both heterologous and homologous strains occur. More than 1 RSV strain may circulate concurrently in a community. However, repeat RSV hospitalizations during one season are rare.

Administration

Palivizumab is to be administered by intramuscular injection only. It is to be given intramuscularly, preferably in the anterolateral aspect of the thigh. Injection volumes over 1 ml should be given as a divided dose.

To administer, remove the tab portion of the vial cap and clean the stopper with 70% ethanol or equivalent. Insert the needle into the vial and withdraw an appropriate volume of solution into the syringe. The gluteal muscle should not be used as an injection site because of the risk of damage to the sciatic nerve. The injection should be given using standard aseptic technique.

Storage

The vial should be kept in the carton to protect it from light. The product should not be mixed with other medicinal products or diluents. Do not shake the vial. It can be stored in a refrigerator (2ºC to 8ºC) but do not freeze. The vial should be inspected visually for particulate matter and discoloration before administration. Do not use any of the vials exhibiting particulate matter or discoloration. The Palivizumab vial contains no preservative and should be administered immediately after drawing the dose into the syringe. Do not re-enter the vial after withdrawal of the drug. Discard unused contents in accordance with local requirements.

Dispensing

Palivizumab is available in 50 mg/0.5 ml and 100 mg /1 ml vials

Palivizumab injection does not have preservatives. So, it should be injected soon after reconstitution. Vials are stored in the refrigerator between 2 to 8 degrees centigrade

Informed consent

Parents should be clearly informed and documented that Palivizumab does not give 100% protection (published studies have shown 30 to 50 % reduction in RSV hospitalization in protected high-risk babies)

Families must be informed that other viral infections like Rhinovirus, COVID-19, and influenza viruses can produce severe respiratory illness, and the "expensive" drug doesn't protect against all respiratory illnesses.

Cost of the drug per season

For a dose of 15mg/kg/dose, a 50 mg vial would suffice for a weight up to 3.5 kg. The MRP of each vial is INR 19,690. With the requirement of 5 doses in an RSV season, the total cost would be Rs. 1,00000 (1 lakh). With an increase in weight, the total cost will also increase.

Questions to be answered

- The targeted population that will give the best cost-benefit needs to be investigated in India
- The season during which the drug must be continued needs to be determined

The position statement would have to be revised after the Nirsevimab / maternal vaccine is available and epidemiologic data becomes available from India

Nirsevimab

Nirsevimab induces higher and longer antibody titers, and it is the currently recommended prophylaxis in the majority of developed countries. Nirsevimab is currently not available in India.

The dose is 50 mg <5 kg and 100 mg >5 kg, and the effect of a single shot persists for up to 150 days against severe RSV-associated lower RTI with high efficacy (78%).

RSV vaccine

RSV vaccine for pregnant women is currently not available in India.

Conflict of interest

The members invited by NNF to prepare the position statement have disclosed lack of conflict to interest or financial association with the pharmaceutical company

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