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Recommendation for immune prophylaxis of respiratory syncytial virus infection in children

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ABSTRACT

Respiratory syncytial virus (RSV) is the most common pathogen for young children hospitalized with bronchiolitis and pneumonia. Most infections occur below 1 year of age, and almost all children have been infected before 2 years of age.

Monoclonal antibodies targeting RSV, such as palivizumab and nirsevimab, are accessible for preventing infection. A committee, consisting of experts in infectious diseases, cardiovascular diseases, and neonatal diseases in children, was assembled by the Pediatric Infectious Diseases Society of Taiwan. Collaborating with the Child Health Research Center at the National Health Research Institutes, Taiwan Pediatric Association, and Taiwan Society of Neonatology, the committee worked to formulate recommendations for immune prophylaxis against RSV infection in children. Palivizumab is recommended for the prevention of RSV infection in high-risk infants under 1 year old with one of the following (1) premature infants with a gestational age <33 weeks, (2) premature infants with a gestational age <35 weeks with chronic lung disease or (3) infants with hemodynamically significant CHD. Nirsevimab is recommended for the prevention of RSV infection in all infants <12 months.

The recommendation is not intended as a sole source of guidance in the prevention of RSV infection in children. The provisions listed in this recommendation are comprehensive suggestions made by pediatric experts in Taiwan based on existing medical evidence. This recommendation should be subject to modification in light of additional medical research findings in the future, and these provisions should not be cited as a basis for dispute resolution.

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1. Introduction

Respiratory syncytial virus (RSV) is the most common pathogen for young children hospitalized with bronchiolitis and pneumonia. Most infections occur below 1 year of age, and almost all children have been infected before 2 years of age.[1,2] Most severe illness affect children within 2–3 months after birth.[3,4]

RSV infection is the leading cause of hospitalization among infants globally.[6–15] About 70 % of infants are infected with RSV in their first year of life, and nearly 90 % children have been infected by age 2 years.[5,15] RSV may account for about 60–80 % of bronchiolitis in infants and up to 40 % of pediatric pneumonias.[5] The mortality is reported to be 0.1 %−9.3 % in hospitalized children.[16,17] A study in Taiwan showed a mortality of 0.8 % in hospitalized children with RSV infection.[2] Although being more frequently observed in preterm infants, most hospitalizations for RSV occur in otherwise healthy young children born at term.[5] RSV is also responsible for a substantial outpatient burden that requires outpatient and emergency department visits.[5]

Epidemiological data suggest that RSV infection in early life may predispose to recurrent wheezing and asthma later in life.[4] However, the causal relationship between RSV infection and the development of asthma is debated.[18] It remains uncertain whether RSV infection is a true predisposing factor to asthma in later life or if RSV bronchiolitis in young children is merely a wheezing episode induced by RSV in children genetically predisposed to atopic diseases. Recent studies suggest that RSV infection is more likely to act as a trigger for a pre-existing predisposition to asthma.[5]

Almost all epidemiological studies indicate that the peak of severe RSV disease occurs in the first 3 months of life.[1,2,4] It seems that maternal antibodies may not effectively protect against the infection. However, passive immunization with RSV monoclonal antibodies and maternal RSV vaccination have proven to be effective,[2,16,19,20] suggesting that the antibodies induced by natural infection may differ in some aspects from monoclonal antibody products and vaccine-induced antibodies, particularly in terms of their neutralizing ability.[21,22]

Chronologic age is the single most important risk factor for severe RSV infection.[23] Severe RSV infection also tends to occurs in children with some certain comorbidities, including prematurity, chronic lung disease (CLD), congenital heart disease (CHD), neuromuscular disorder, major respiratory tract anomaly, and immune compromised condition.[2,23]

The comorbidity with the greatest risk for severe RSV infection is prematurity. Preterm infants with a gestational age of <29 weeks have RSV hospitalization rates 2 to 4 times higher than later preterm infants.[1] The risk of severe infection decreases with increasing gestational age.[1] Data regarding the risk of severe RSV infection in preterm infants born at 29 to <35 weeks' gestation are controversial. Some studies claim an increased risk of RSV hospitalization in preterm infants born at 29 to <35 weeks' gestation, while other studies do not reach the same conclusion.[23]

Nosocomially acquired infections are also significant predictors for the need for intensive care.[2] A global study showed that the proportion of RSV-related nosocomial deaths among all RSV deaths was lower in low- and lower-middle-income countries than in upper-middle-income countries and high-income countries.[24]

A meta-analysis showed that among the risk factors for severe RSV infections, only prematurity with a gestational age <37 weeks is significantly associated with mortality.[16] However, a study in Taiwan demonstrated that the presence of CHD, especially acyanotic CHD, was significantly associated with a fatal outcome.[2]

RSV is divided into two subtypes, A and B, based on the glycoprotein G sequence. RSV is continuously evolving leading to the emergence of new genotypes. Gene mutations mostly occur in the RSV G gene, whereas the F gene sequence is highly conserved and therefore is often the target of anti-RSV monoclonal antibodies for prophylactic use. Despite the potential emergence of escape mutants, prophylactic use of palivizumab has not been reported to be associated with major mutations.[5] Many countries have established guidelines for the immune prophylaxis of RSV.[1,25] Due to the varying seasonal distribution of RSV across different countries, we have developed these guidelines based on the local epidemiological patterns in Taiwan. These recommendations could also serve as a reference for countries with climates similar to that of Taiwan.

2. Recommendation 1: general preventive measures

1.1 Breast milk contains immune globulins and other immune factors that counteract RSV. Breastfeeding can reduce the infection rate and severity of RSV-related diseases.

1.2. Hand contamination is a crucial transmission route for RSV, including infections related to healthcare. It is essential to wash hands thoroughly before and after contacting patients, handling equipment around patients, and removing gloves. The use of certified dry hand sanitizers is recommended. If hands are visibly soiled or if dry hand sanitizers are unavailable, wet hand washing is necessary.

1.3 Secondhand smoke can increase the risk and severity of RSV infections. Family members should avoid smoking.

Human milk may provide antibodies, and some antimicrobial and immune modulating substance that may protect infants from many infections, including RSV bronchiolitis.[4] Some studies suggest that breast milk may decrease the incidence of respiratory tract infections, and the effect may last for several years beyond infancy.[18,26,27] The Taiwan Pediatric Association recommends exclusive breastfeeding for 4–6 months after birth.[28]

RSV is transmitted through aerosol droplets or by direct/indirect contact with contaminated objects.[4] RSV, like many other viruses, may remain viable and infectious for minutes to hours after leaving the human body.[29,30] It can spread to others through direct contact or indirectly by acquiring the virus through touching contaminated fomites. In-facility transmissions of RSV primarily occur through the contaminated hands of caregivers.[30] All caregivers should disinfect their hands before and after direct contact with RSV-infected patients, handling inanimate objects around patients, and after removing gloves.[30] RSV is susceptible to alcohol-based hand rubs, which are the preferred method for eliminating RSV from contaminated hands. Hand washing with soap or other antiseptic agents and water is necessary when hands are visibly soiled.[30] Tobacco smoke exposure may predispose to bronchiolitis.[30] Secondhand smoke should be avoided.

3. Recommendation 2: palivizumab

2.1 The dose is 15 mg/dose, intramuscular injection once a month. As there is no distinct RSV season in Taiwan, it is recommended to continue the use of palivizumab for a certain period after birth. The Taiwan National Health Insurance suggests its use for up to 6 months post-birth.

2.2 Palivizumab is recommended for the prevention of RSV infection in the following high-risk infants under 1 year old:

- 2.2.1 Premature infants with a gestational age <33 weeks.
- 2.2.2 Premature infants with a gestational age <35 weeks with chronic lung disease.
- 2.2.3 Infants with hemodynamically significant CHD.

2.3 Palivizumab may be considered for the prevention of RSV infection in at-risk infants below 1 year of age, including:

- 2.3.1 Infants at risk for recurrent pneumonia due to respiratory tract abnormalities or neuromuscular diseases.
- 2.3.2 Infants with severe immunodeficiency.

2.3 Palivizumab can be administered concurrently with other vaccines at different sites, including all inactivated and live attenuated vaccines.

2.4 Contraindications: Severe allergy to palivizumab or its components, including immediate-type hypersensitivity reactions such as anaphylaxis.

2.5 If the mother received the RSV vaccine (RSVpreF, Pfizer) between weeks 32–36 of pregnancy and the interval between vaccine administration and delivery has been ≥14 days, palivizumab injection may not be needed.

Palivizumab (Synagis, AstraZeneca) is a humanized mouse immunoglobulin (IgG1) monoclonal antibody targeting the fusion (F) protein of the virus. The antigenic site is preserved on both the pre-fusion and post-fusion conformations of the F protein.[5,23] The amino acid sequences are 95 % of human origin, while 5 % (antigen binding sites) are of mouse origin.[23] The half-life is 19–27 days, requiring monthly injections to maintain protection against RSV infection (Table 1).[5]

The IMpact-RSV trial demonstrated an absolute reduction of 5.8 % in RSV hospitalizations in young infants.[23] Another study on children with hemodynamically significant CHD showed an absolute reduction in the RSV hospitalization rate of 4.4 % (Table 1).[23] Palivizumab was shown to be safe and well-tolerated in both of these studies. A study in Taiwan utilized a 6-monthly-dose palivizumab in 127 preterm infants, including 108 infants born at ≤ 28 weeks and 19 infants born at 29–35 weeks with CLD. The reduction in RSV-related hospitalization rates was 86 % within 6 months after discharge.[19] A Cochrane review concluded that palivizumab is effective and safe but failed to demonstrate a mortality benefit.[31]

Table 1
Summary of the differences between palivizumab and nirsevimab.

	Palivizumab	Nirsevimab
Mechanism of action	Humanized mouse immunoglobulin monoclonal antibody targeting the RSV fusion protein	Recombinant, human monoclonal antibody binding to the F1 and F2 subunits of the F protein of the RSV
Administration frequency	Once per month	Single dose
Dosage	15 mg/dose	For aged <8 months with body weight <5 kg: 50 mg/dose For body weight ≥5 kg: 100 mg/dose For aged ≥8 months: 200 mg/dose
Target population	1. High-risk infants under 1 year old (1) Prematurity with a gestational age <33 weeks (2) Premature infants with a gestational age <35 weeks with chronic lung disease (3) Hemodynamically significant CHD 2. At-risk infants below 1 year old (1) At risk for recurrent pneumonia due to respiratory tract abnormalities or neuromuscular diseases (2) Severe immunodeficiency	1. All infants <12 months 2. Children ≥12 months and <24 months with risk factors for severe RSV infection (1) Prematurity with CLD requiring special medical care in the past 6 months (including ongoing steroid therapy, diuretics, oxygen therapy) (2) Hemodynamically significant CHD (3) At risk for recurrent pneumonia due to respiratory tract abnormalities or neuromuscular diseases (4) Severe immunodeficiency
Clinical efficacy[23,51]	1. Reduction of 5.8 % in RSV hospitalizations in young infants 2. Reduction of 4.4 % in RSV hospitalization in children with hemodynamically significant CHD	1. Efficacy against hospitalized RSV-associated lower respiratory tract infection was 83.2 % 2. Efficacy against very severe RSV-associated lower respiratory tract infection was 75.7 %

Abbreviations: RSV, respiratory syncytial virus; CHD, congenital heart disease; CLD, chronic lung disease.

RSV is an RNA virus with an inherent tendency for frequent mutation. RSV escape mutants resistant to palivizumab have been reported in approximately 5 % of children experiencing breakthrough RSV infection while receiving monthly palivizumab prophylaxis.[24] Some investigations reported that natural gene polymorphism involving the F protein of RSV occurred even without palivizumab usage, and the palivizumab neutralization resistant mutations rate was 0.7 %.[32,33] However, the effectiveness of palivizumab for the prevention of RSV infection has persisted until recently. Continuous monitoring of the trends in RSV genetic variations, as well as an analysis of their impact on the efficacy of palivizumab in prevention is needed.

In temperate areas, RSV predominantly circulates during cold seasons, typically between November and March in the Northern Hemisphere.[2] In equatorial countries, RSV causes disease throughout the year, with increased activity associated with rainfall and an inconsistent relationship with temperature.[2] Taiwan is located in a subtropical area, and RSV infections occur throughout the year. A study indicated that the monthly distribution of RSV infections in Northern Taiwan exhibited a bimodal pattern, with one peak from March to May and another from August to October. In Southern Taiwan, the distribution showed a single peak from April to July, with considerable year-to-year variations.[2] Recent epidemiological data from 2017 to 2019 in Taiwan showed that RSV predominantly circulated during July and October with a peak in August.[9] After the COVID-19 pandemic, RSV cases were rare in 2021. However, RSV began circulating in August and reached its peak during November and December in 2020 and 2022.[9,34] Due to the difficulty in defining a consistent RSV season in Taiwan, palivizumab is recommended to be administered for a specific period after birth, rather than during "RSV season." The Joint Committee on Vaccination and Immunization in UK also advises a preference for a year-round offer for a passive immunization program to ensure high uptake and for reasons of operational effectiveness because this would be less complex and resource intensive to deliver, compared with running seasonal campaigns.[25]

American Academy of Pediatrics (AAP) recommends 5 monthly doses of palivizumab, which may provide more than 6 months of serum palivizumab concentrations above the desired level.[1] As there is no consistent RSV season in Taiwan, we recommend 6 monthly doses of palivizumab to be administered shortly after birth, regardless of the birth month. Anaphylaxis has been reported after palivizumab injection, including both initial and repeated administration.[1] The occurrence of severe hypersensitivity reactions precludes the continued use of palivizumab. Similar to other vaccines, palivizumab can be administered simultaneously with live or inactivated vaccines.[1]

Initially, AAP advised the use of palivizumab in infants born at 32 weeks of gestation or earlier.[25] The 2014 AAP advised against use of palivizumab for healthy infants ≥29 weeks' gestation.[1,35] There were several studies evaluating the effect of this guideline modification. Some studies suggested an increased risk of RSV hospitalization in infants of 29–32 weeks' gestation.[1,22,35] A study compared RSV hospitalization rates in children less than 24 months of age from the 2 years before to the 1 year after the guideline change. No significant difference was found between the 2 periods in RSV hospitalization rate.[36] This conclusion may be confounded by that most severe RSV infections occur within 3 months after birth. Analyzing data from children younger than 24 months may dilute the real difference between groups. Because some other studies also reached a similar conclusion, AAP keep their recommendation unchanged in the updated guideline in 2023.[1]

The Impact-RSV study report in 1998 demonstrated that the rate of RSV hospitalizations associated with palivizumab administration was significantly lower in infants with prematurity ≤35 weeks without other comorbid conditions.[37] Another study indicated that the use of palivizumab in healthy preterm infants born at a gestational age of 33–35 weeks resulted in a relative reduction of 61 % in the total number of wheezing days during the first year of life.[38] The committee concludes that preterm infants with a gestational age >29 weeks and <33 weeks

are at a significantly higher risk for severe RSV infection compared to term infants, and the use of palivizumab in this group may be beneficial. Therefore, the present recommendation for palivizumab use includes all healthy preterm infants born at < 33 weeks rather than <29 weeks.

The presence of CLD in preterm children is a significant factor for severe RSV infection.[1,2] The elevated risk continues through the second year of life.[1] Studies have shown that palivizumab is effective in reducing the incidence of severe RSV infection in this group of infants, including those in the second year of life.[1] Our recommendation for palivizumab use in preterm infants with CLD aligns with the recommendation made by AAP,[25] except that we recommend prophylaxis in preterm infants born at < 35 weeks rather than <32 weeks.

It is generally agreed that CHD may predispose individuals to severe RSV infection.[2,25] A study in Taiwan demonstrated that CHD is also a significant risk factor for fatal RSV infection, especially acyanotic CHD.[2] RSV hospitalizations in children with hemodynamically significant CHD have been decreasing after the use of palivizumab.[1] One study suggested that palivizumab prophylaxis has less benefit in cyanotic children than in acyanotic children.[1] The benefit of palivizumab use for children with CHD during the second year of life is controversial. Some studies suggested its effectiveness, while others did not.[1] We recommend the use of palivizumab in this group of children only during the first year of life.

The risk of severe RSV infection has not been well defined in children with neuromuscular disorders and major respiratory tract anomalies that may impair the ability to clear respiratory secretions, such as congenital pulmonary airway malformation, congenital diaphragmatic hernia, severe neurological disorders compromising respiratory function, tracheoesophageal fistula, lung hypoplasia, and conditions requiring tracheostomy or ventilator support.[1] The susceptibility to severe lower airway disease may increase with age due to the progressive nature of some neuromuscular diseases. Children with major neuromuscular disorders are, therefore, at risk for severe RSV infections even as they age.[23] One study in Taiwan suggested that neuromuscular disease is a significant risk factor for severe RSV infection.[2] It is challenging to objectively assess the severity of these disorders and the potential benefit of using palivizumab due to the considerable variability in the severity of these anomalies. We choose to define this group of infants who may benefit from the use of palivizumab based on the risk of recurrent pneumonia.

Immunocompromised children and adults are prone to suffer from severe RSV infections that may be fatal.[1,2] Lymphopenia and impaired T-cell function are key determinants of severe illness.[1] Palivizumab is not effective to RSV infection in infected patients.[1,23] Due to the relatively low prevalence of immunocompromised conditions, there is insufficient data to conclusively support or refute the potential benefits of immunoprophylaxis in this patient group.[1] Given that immunocompromised status is a significant risk factor for severe RSV infection and palivizumab may help prevent such infections, the committee suggests considering the use of this agent in immunocompromised children. This recommendation aligns with the guidance provided by AAP.

RSV reinfection likely occurs due to the virus's frequent mutation and suboptimal human immune responses.[1,39] Repeat RSV hospitalizations within a single season are considered rare.[23] A study spanning eight successive RSV seasons identified 726 RSV infections, including just one case of repeated infection, among 1560 children.[40] Repeat RSV infections generally result in milder clinical manifestations compared to primary RSV infections.[23,39] For these reasons, the AAP recommends discontinuing palivizumab prophylaxis for children who experience breakthrough RSV hospitalization.[1]

Most studies on RSV reinfection are not limited to young infants,[23,41] which may underestimate the true incidence of breakthrough infection. A 10-year study of normal children followed longitudinally from early infancy revealed that RSV reinfection is not infrequent.[39] As mentioned before, maternal antibodies may not effectively protect against RSV infection in young infants, while palivizumab and maternal RSV vaccination can.[2,16,19,20,42] This phenomenon can be attributed to the fact that monoclonal antibody products and antibodies elicited by RSV vaccines target only the pre-F protein, whereas natural infection induces both neutralizing pre-F antibodies and non-neutralizing post-F antibodies. Studies have shown that post-F antibodies are ineffective for prevention[22,43] and may even be associated with RSV vaccine-enhanced disease.[44] This could explain why frequent reinfections are common in RSV infections, as natural immunity is weaker compared to the immunity provided by monoclonal antibodies specifically targeting the pre-F protein. Consequently, palivizumab may function differently from naturally occurring antibodies. The committee, therefore, recommends the continued use of palivizumab in indicated individuals even after breakthrough RSV infections.

RSV hospitalizations occur less frequently during the second year of life. A prospective study indicated that 75 % of RSV hospitalizations occurred in children younger than 12 months.[23] There are no efficacy data regarding palivizumab prophylaxis in the second year of life.[23] The committee does not recommend the use of palivizumab beyond 12 months of age. A systematic review of studies primarily from the USA and Canada found that Palivizumab prophylaxis for RSV may be cost-effective for certain infant subgroups. However, its cost-effectiveness varied depending on the study setting, population, risk factors, and input parameters. Palivizumab was deemed cost-effective for preterm infants, those with lung complications, and infants from remote communities.[45]

4. Recommendation 3: nirsevimab

- 3.1 Administered as a single dose via intramuscular injection. As there is no distinct RSV season in Taiwan, it is recommended to administer a single dose shortly after birth, regardless of the season of birth.
- 3.2 Nirsevimab is recommended for the prevention of RSV infection in the following groups:
  - 3.2.1 All infants <12 months, preferably administered shortly after birth. For children aged <8 months with body weight <5 kg, the dosage is 50 mg, and for body weight ≥5 kg, the dosage is 100 mg. For children ≥8 months, the dosage is 200 mg, divided into two injections of 100 mg each, simultaneously at different sites.
  - 3.2.2 Children ≥12 months and <24 months with risk factors for severe RSV infection, administer an additional dose of 200 mg, divided into two injections of 100 mg each, simultaneously at different sites. High-risk factors include:
    - 3.2.2.1 Prematurity with CLD requiring special medical care in the past 6 months (including ongoing steroid therapy, diuretics, oxygen therapy).
    - 3.2.2.2 Hemodynamically significant CHD.
    - 3.2.2.3 At risk for recurrent pneumonia due to respiratory tract abnormalities or neuromuscular diseases.
    - 3.2.2.4 Severe immunodeficiency.
- 3.3 Nirsevimab can be co-administered with other vaccines at different sites, including all inactivated and live attenuated vaccines.
- 3.4 Contraindications: Severe allergy to nirsevimab or its components, including anaphylaxis.
- 3.5 If the mother received an RSV vaccine (RSVpreF, Pfizer) between weeks 32–36 of pregnancy, and the interval between vaccination and delivery is ≥ 14 days, administration of nirsevimab may not be needed.

Nirsevimab (Beyfortus, Sanofi and AstraZeneca) is a recombinant, human monoclonal antibody that binds to the F1 and F2 subunits of the F protein of the RSV to prevent infection.[31] It contains a three amino acid substitution in the Fc region, resulting in an extended half-life of 63–73 days in infants (Table 1).[5,46] It is active against both RSV subtypes A and strains, and the binding site was highly conserved.[5] Nirsevimab escape

variants were very rare and have not increased over time.[47] The prevalence of RSV A or RSV B strains containing nirsevimab binding-site substitutions were <1 % in every RSV season between 2015 and 2021.[48] Adverse reactions were similar between nirsevimab and placebo.[23] Anti-nirsevimab antibodies were observed in 5.6 % of infants receiving nirsevimab versus 3.8 % of those receiving placebo.[5]

The RSV neutralizing antibody level may remain over 7-fold higher than baseline on day 361 after nirsevimab injection.[46] The antibody level against the post-fusion RSV F protein is comparable between nirsevimab recipients and placebo recipients. This suggests that while nirsevimab may be effective in providing protection against symptomatic RSV disease, it may not prevent all subclinical infections.[46]

Protective efficacy was evaluated through 150 days after injection in phase IIb (1453 preterm infants with a gestational age of 29–34 weeks) and phase III studies (3012 late preterm and term infants with a gestational age ≥35 weeks).[49,50] Pooled efficacy for medically attended RSV-associated lower respiratory tract infection (LRTI) was 79.0 % (95 % confidence interval [CI] = 68.5%–86.1 %). Pooled efficacy for hospitalized RSV-associated LRTI was 80.6 % (95 % CI = 62.3%–90.1 %), and pooled efficacy for RSV-associated LRTI with ICU admission was 90.0 % (95 % CI = 16.4%–98.8 %). No fatal cases attributable to RSV were reported in these trials. The incidence of serious adverse events was not increased after nirsevimab use.[49,50]

The Phase IIIb nirsevimab study included infants aged ≤12 months with a gestational age of ≥29 weeks. The protective efficacy against hospitalized RSV-associated lower respiratory tract infection was 83.2 % (95 % CI = 67.8%–92.0 %). Additionally, the protective efficacy against very severe RSV-associated lower respiratory tract infection was 75.7 % (95 % CI = 32.8%–92.9 %) (Table 1).[51] A post-marketing matched case-control study showed that the protective effectiveness of nirsevimab against hospitalization for RSV-associated bronchiolitis in infants less than 12 months was 83.0 % (95 % CI = 73.4%–89.2 %) in a real-world setting.[52]

The cost-effectiveness analysis for the use of nirsevimab in infants aged <8 months (at USD 445 per dose) was estimated to be USD 102,811 per quality-adjusted life year, suggesting potential cost-effectiveness.[15] However, the use of nirsevimab for all children entering their second RSV season (at USD 890 per dose) was estimated to be USD 1,557,544 per quality-adjusted life year, indicating that it may not be cost-effective.[15] Another study evaluated the cost-effectiveness of Nirsevimab among infants aged 0–7 months and those 8–19 months old concluded that Nirsevimab for infants may be cost effective particularly among those with higher risks and costs of RSV. Nirsevimab in the second season for children facing a 10-fold higher risk of hospitalization would cost USD 308,469 per quality-adjusted life year saved.[53]

Advisory Committee on Immunization Practices of the United States and AAP recommend 1 dose of nirsevimab (100 mg) for all infants aged <8 months born during or entering their first RSV season. One dose of nirsevimab (200 mg) is also recommended for infants and children aged 8–19 months who are at increased risk for severe RSV disease and entering their second RSV season.[15,54]

We recommend administering nirsevimab to all children shortly after birth, guided by cost-effectiveness studies. While the cost-effectiveness in children at high risk for severe RSV infection during the second year of life has not been fully evaluated, the committee believes that these children may derive benefits from nirsevimab. This includes children with prematurity-associated chronic lung disease (CLD) requiring special medical care in the past 6 months, hemodynamically significant congenital heart disease (CHD), a risk of recurrent pneumonia due to respiratory tract abnormalities or neuromuscular diseases, and those with severe immunodeficiency.

In accordance with general best practices for immunization, nirsevimab can be given at the same time with other vaccines.[15] There was not a significant safety concern of nirsevimab, and the only contraindication for its use is a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a product component.[15]

CRediT authorship contribution statement

Ping-Ing Lee: Writing – review & editing, Writing – original draft, Conceptualization. **Yhu-Chering Huang:** Supervision, Conceptualization. **Chih-Jung Chen:** Conceptualization. **Cheng-Hsun Chiu:** Formal analysis, Data curation. **Po-Yen Chen:** Conceptualization. **Chun-Yi Lu:** Formal analysis, Data curation. **Ching-Chuan Liu:** Formal analysis, Data curation. **Nan-Chang Chiu:** Formal analysis, Data curation. **Hsin Chi:** Formal analysis, Data curation. **Chien-Yu Lin:** Formal analysis, Data curation. **Chun Yi Lee:** Formal analysis, Data curation. **Shuenn-Nan Chiu:** Formal analysis, Data curation. **Mei-Jy Jeng:** Formal analysis, Data curation. **Kuang-Che Kuo:** Formal analysis, Data curation. **Ren-Bin Tang:** Formal analysis, Data curation. **Yung-Feng Huang:** Formal analysis, Data curation. **Hui-Hsien Pan:** Formal analysis, Data curation. **Ming-Fang Cheng:** Formal analysis, Data curation. **Li-Min Huang:** Supervision, Methodology. **Ya-Li Hu:** Writing – review & editing. **Tzou-Yien Lin:** Supervision.

Declaration of competing interest

The authors declared no conflicts of interest.

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