

## Summary

Introduction: Respiratory syncytial virus (RSV) is a significant cause of lower respiratory tract infections in young children, causing infection in almost every infant before the age of two. The highest risk of severe course of the disease occurs in preterm infants, especially in children with bronchopulmonary dysplasia (BPD) but also with those who suffer from hemodynamically significant congenital heart disease. The only possibility of preventing infections caused by this pathogen is immunoprophylaxis based on palivizumab.

Objective: The main objective of the doctoral dissertation, based on three original publications, was to evaluate the effectiveness of the nationwide prophylaxis program using palivizumab over six seasons, that is periods covering several months in which the highest risk of RSV infection is recorded (2008-2014).

The specific objectives presented in the discussed works included:

1. Evaluation of the use and compliance of immunoprophylaxis with regard to the applicable criteria.
2. Assessment of health outcomes and palivizumab supply tolerance.
3. Assessment of adherence to immunoglobulin dosing regimen recommendations, identification of factors that could influence parental compliance, and comparison of data with analogues from other countries.
4. Evaluation of the incidence of BPD in the group of children born before 28 weeks of gestational age in 2013, qualified for prophylactic treatment.

Material and methods: A retrospective analysis of data on children enrolled in the prevention program in 2008-2014 who received at least one dose of palivizumab financed by the Polish National Health Fund was conducted. The evaluation included: the course of the neonatal period, sociodemographic factors, the presence of other diseases, details of palivizumab administration, and compliance with palivizumab dosing recommendations. In the group of children born before 28 weeks of gestational age in 2013, who were qualified for the prevention program in the seasons 2012-2013 and 2013-2014, the necessity to use oxygen therapy for at least 28 days and in the 36<sup>th</sup> week of the corrected age was assessed, counting from the date since the last menstruation.

Results: The prophylaxis program covered 3,780 children aged 4 weeks to 2 years. In individual seasons, the number of children ranged from 464 to 995. During the program, the children received an average of 3.8 injections (range 1 to 5 doses). Adverse events occurred after 392 doses of palivizumab and accounted for 2.7% (392/14275). Anxiety was

the most common (1.2%). The highest mean number of injections was recorded in the 2013/14 season ( $4.3 \pm 1$ ), and the lowest one in the 2009/10 season ( $2.7 \pm 0.8$ ).

A group of 3,084 children (81.7%) received all the expected doses, while 2,352 (62.2%) children received subsequent injections within the appropriate time intervals. The lowest compliance was observed in the first two immunization seasons. Male children were more likely to be non-compliant. There was also a significant relationship between compliance, defined as the administration of all expected doses, and the age at the time of initiation of immunization. None of the other demographic, social or clinical factors appeared to influence adherence.

As part of the drug program, a group of 603 children born before 28 weeks of gestational age in 2013 received palivizumab. According to the Central Statistical Office data on births and mortality rates in Poland in 2013, this group accounted for 87.8% of the population meeting the criteria for inclusion in the program. Bronchopulmonary dysplasia was diagnosed in 80.9% of infants born before 28 weeks of gestation, with mild BPD in 70.7% of cases. Gestational age, birth weight and under-birth weight in relation to gestational age were found to be significant risk factors for BPD.

#### Conclusions:

1. The RSV infection prophylaxis program with palivizumab in the population of preterm infants and those with BPD is conducted effectively and in accordance with the applicable criteria.
2. The supply of immunoglobulin is a safe procedure and the incidence of adverse events is low.
3. The degree of compliance with the recommendations observed in the Polish population is similar to data from prevention programs conducted in other countries. As boys were the subpopulation with a higher likelihood of non-compliance, this should be taken into account in the process of educating about the effects of non-adherence to dosing and reinforced in the physician-parent communication.
4. Data reported during this prevention program can be a valuable source of information on the incidence of BPD as well as identifying risk factors for this significant complication of respiratory system in preterm infants.