1.0 Abstract

Title: A One-Year Observational Study of Palivizumab in Infants at Risk for Respiratory Syncytial Virus Infection in Latin America

Keywords: Respiratory syncytial virus, palivizumab, hospitalization, compliance.

Rationale and Background: Despite the high morbidity that respiratory syncytial virus (RSV) represents in Latin America, relatively little is known about the current use, compliance and effectiveness of palivizumab in high-risk infants.

Research Question and Objectives: The objectives of this clinical study were to describe patterns of palivizumab usage in high risk-infants in Latin America; to estimate the RSV hospitalization rate during a follow-up period of 1 year after the first dose and to determine the palivizumab compliance rate of the indication.

Study Design: Prospective, observational, multi-center cohort study.

Setting: Infants at risk for RSV infection with at least one dose of palivizumab prescribed according to local guidelines were included in seven countries from Latin America

Subjects and Study Size, including dropouts: 458 children were enrolled in 24 sites of 7 countries within Latin America. 397 infants (86%) completed follow up. Subject recruitment commenced on February 19th 2011 and concluded on September 6th 2012. Seasonality coverage was variable due to different country epidemiological patterns.

Variables and Data Sources: Epidemiological and clinical data was collected through visits or phone calls during one year after receiving the first dose of palivizumab.

Results: 458 children were enrolled in 24 sites of 7 countries: 52% were male, mean birth weight was 1345g (SD: 460), median gestational age was 31 weeks (range: 23-39). 449 children (98%) were premature, 129 (29%) had bronchopulmonary dysplasia (BPD) and 46 (10%) had congenital heart disease. 397 infants (86%) completed follow up. Prophylaxis compliance (measured as received vs estimated doses) was 83.6%. Fifty two children required admission due to lower respiratory infection (sixty one episodes). Hospitalization rate due to lower respiratory tract infection (LRTI) was 14.58 per 100 patient-years(95% CI:10.51-18.65). RSV infection was confirmed in 12 episodes.

In 147 patients from one country with low compliance rate (61%) of the indicated dosage the hospitalization rate due to LRTI was 19.29 per 100 patient-years (95% CI: 11.4-27.1). Twenty two hospitalizations due to respiratory disease were registered in 21 of the 147 patients . RSV etiology was confirmed in 5 episodes

In a subgroup of 134 children with bronchopulmonary dysplasia, hospitalization rate due to LRTI was 26.4 per 100 patient years (95% CI: 17.1-35.8). RSV related hospitalization rate was 7.44 per 100 patient years.

After risk factor analysis, the only variable that increases the risk of hospitalizations due to lower respiratory tract infection in this study was bronchopulmonary dysplasia. Incidence risk ratio for children with BPD was 2.7 (95% CI: 1.6-4.5).

Three deaths not related with the drug or with confirmed RSV were registered during follow up for those tested for RSV. There were no serious adverse events related to the administration of palivizumab in this study.

Conclusion:

- According to our knowledge, this is the first study regarding patterns of use and outcomes associated with palivizumab in LA.
- Prematurity was the most frequent cause of palivizumab indication (98% of the cases) in the 7 countries involved in the study.
- There were 61 episodes with hospitalization related to lower respiratory tract infections in 52 infants (rate: 14.58 per 100 patient years). RSV LRTI was confirmed in 12 episodes.
- Prophylaxis compliance (received vs expected doses) rate was 83.6%.
- Bronchopulmonary dysplasia was the only risk factor for hospitalization due to lower respiratory tract infection.
- There were no new significant safety concerns identified. The adverse events reported in Latin America were consistent with the known safety profile of palivizumab.